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Novel paracetamol-based, stable, liquid formulation in an aqueous solvent.

Also see claims 1-27 (highlighted)

Inventor: Dietlin et al.

STAFF USE ONLY

Date completed: 3-1-99

Searcher: JOHN DAVIDSON

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	A.A. Sequence		SDC
	Structure		DARC/Questel
✓	Bibliographic		Other

=> D L27 BIB ABS

L27 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:194495 HCAPLUS
DN 126:242676
TI Interaction of supercritical fluids with drug/cyclodextrin inclusion compounds and physical **mixtures**
AU Giordano, F.; Rillosi, M.; Bettinetti, G.P.; Gazzaniga, A.; Majewski, W.; Perrut, M.
CS Pharmaceutical Department Viale delle Scienze 78, Parma, 43100, Italy
SO Proc. Int. Symp. Cyclodextrins, 8th (1996), 193-196. Editor(s): Szejtli, J.; Szente, L. Publisher: Kluwer, Dordrecht, Neth.
CODEN: 64CDAL
DT Conference
LA English
AB The interaction of supercrit. carbon dioxide with a model drug (acetaminophen)/.beta.-cyclodextrin system, tested as solid **mixt** . or as inclusion compd., was investigated. The influence of temp., particle size and **water** content on the interaction behavior was also assessed. The inclusion compd. proved to be fairly **stable** in the exptl. conditions adopted.

=> D L27 BIB ABS 2-6

L27 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 1999 ACS
AN 1990:558691 HCAPLUS
DN 113:158691
TI Pharmaceutical **composition** containing a slightly **water** -soluble active substance and a glyceride gelled with a cellulose polymer
IN Aiache, Jean Marc
PA Fr.
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 356325	A1	19900228	EP 89-402306	19890818
	EP 356325	B1	19940504		
	R: AT, BE, CH, DE, ES, GB, GR, IT, LI, LU, NL, SE				
	FR 2635463	A1	19900223	FR 88-11037	19880819
	AT 105193	E	19940515	AT 89-402306	19890818
PRAI	FR 88-11037	19880819			
	EP 89-402306	19890818			

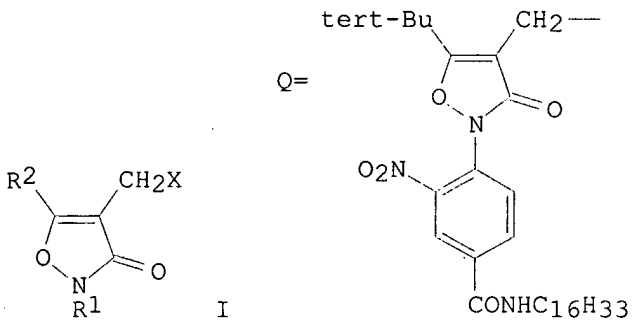
AB **Stable** pharmaceutical **compns**. for oral, topical or parenteral administration comprise a low-soly. drug, incorporated, at .ltoreq.25%, in glyceride(s) gelled with cellulose polymer(s). A **mixt**. of 3800 g Labrafil (glyceride) and 200 g Et cellulose was heated at 150.degree. to give a clear liq., which was cooled to 30.degree.
and blended with 280 g doxycycline hyclate to give a drug **compn**.

L27 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 1999 ACS
AN 1990:459160 HCAPLUS
DN 113:59160
TI Preparation of isoxazol-3-one derivatives as reagents for protecting acids

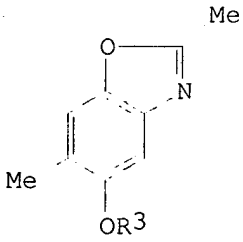
IN Ito, Takayuki; Nakamura, Takeki
PA Fuji Photo Film Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02049776	A2	19900220	JP 88-200603	19880811

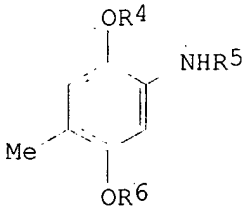
OS MARPAT 113:59160
GI



I



II



III

AB The title compds. (I; X = halo, sulfonyloxy; R1,R2 = H, substituent; provided that at least one of R1 and R2 is NO2-substituted aryl or heterocyclyl) are prepd. and can be used to protect proton acids having pKa .ltoreq.15, e.g. phenols, carboxylic acids, and sulfonic acids, under mild conditions to form groups **stable** under weakly basic to acidic conditions, while the selective deprotection is effected by redn. or photochem. redn. under a neutral condition. Thus, a **mixt.** of N-methyl-N-hexadecyl-3-nitro-4-chlorobenzenesulfonamide, 5-tert-butyl-3-hydroxyisoxazole, K2CO3, and DMSO was heated 6 h at 60.degree. to give 100% 5-tert-butyl-2-(4-N-methyl-N-hexadecylsulfamoyl-2-nitrophenyl)isoxazolin-3-one which was treated with paraformaldehyde in refluxing AcOH contg. ZnCl2 under a stream of HCl (g) to give 3-oxoisoxazol-4-ylmethyl chloride, i.e., QCl. Versatility, stability, and selectivity of the protecting group Q for phenolic OH groups was demonstrated; e.g. treatment of 5-hydroxybenzoxazole deriv. (II; R3 = H) with QCl in refluxing Me2CO contg. K2CO3 and KI, hydrolysis of the product

II (R3 = Q) with refluxing 12N **aq.** HCl and EtOH to dihydroxyaniline III.HCl (R4 = R5 = H, R6 = Q), and successive acylation of the latter with (Me3CO2C)2O and Ac2O in pyridine gave III (R4 = Ac, R5 = CO2CMe3, R6 = Q). Treatment of the latter with trimethylhydroquinone and Et3N in DMF at 10-25.degree. gave 75% III (R4 = Ac, R5 = COCMe3, R6 = H).

L27 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 1999 ACS
AN 1989:179558 HCAPLUS
DN 110:179558
TI Preparation of inclusion compounds of cyclodextrin ethers with lipophilic drugs
IN Pitha, Josef
PA United States Dept. of Health and Human Services, USA
SO U.S., 7 pp. Cont.-in-part of U.S. 4,596,795.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

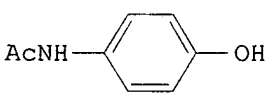
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4727064	A	19880223	US 85-738749	19850529
	US 603839	A0	19840831	US 84-603839	19840425
	US 4596795	A	19860624		
PRAI	US 84-603839		19840425		

AB Inclusion compds. of a cyclodextrin-based **mixt.** and a drug with a substantially low **water**-soly., are prepd. to improve dissoln. properties of the drug and hence its absorption by the body. Hydroxypropyl .beta.-cyclodextrin was prepd. by treating .beta.-cyclodextrin with propylene oxide in alk. media. The soly. of estradiol in **aq.** soln. contg. 40% hydroxypropyl .beta.-cyclodextrin was 28.0, compared to <1.6 mg/mL in **water.** Hydroxypropyl .beta.-cyclodextrin with medium degrees of substitution (5-7) was more effective solubilizer than that of higher degrees of substitution. The solns. of drugs in cyclodextrins were **stable** when kept at room temp. for several months and no microbial growth in the solns. was obsd.

L27 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 1999 ACS
AN 1984:598212 HCAPLUS
DN 101:198212
TI Free-flowing paracetamol granules
IN Noeltner, Gerhard
PA Hoechst A.-G. , Fed. Rep. Ger.
SO Ger. Offen., 15 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3306012	A1	19840823	DE 83-3306012	19830222

GI



I

AB Free-flowing paracetamol (I) [**103-90-2**] granules are prepd. by fluidized-bed granulation and consist of 2-20% starch [9005-25-8] or 1-50% hydroxypropyl Me cellulose [**9004-65-3**]. The I granules are not discolored, are storage-**stable** and are suitable for tableting. Thus, in a fluidized-bed granulation app., 20 kg I was sprayed with corn starch soln. The granulate obtained was sprayed with 10% corn starch suspension and pulverized and sieved. The particle size of the granulate was detd. The final **compn**. of the suspension was I 5.4, treated corn starch 0.48, corn starch 0.12 and **water** 6.0 kg.

L27 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 1999 ACS
AN 1971:59385 HCAPLUS
DN 74:59385
TI Stabilizing or fixing images obtained with organic photosensitive **compositions**
IN Yamada, Yoshikazu; Storm, Lester F. M.
PA Bell and Howell Co.
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3544321	A	19701201	US 66-566731	19660721

AB Images formed by imagewise exposure to actinic light of a photosensitive combination of an org. halide and an aromatic N-atom-contg. compd. are stabilized by one of the compds. contg. a substituted phenoxy group. Thus, a film was prepd. with a **compn**. contg. 20% **aq**. gelatin 50 ml, N-vinylcarbazole 2.5 g, CBr4 0.75 g, EtOAc 1.5 ml, aerosol OT 8 drops, formalin 1 drop, dried, exposed, developed and dipped in an **aq**. soln. of 4% hydroquinone monomethyl ether and 2% Na2S2O5 for 5 min, then dried. The background areas remained light after 2 hr exposure in a fadometer.

=> D L25 BIB ABS HITRN

L25 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1999:7930 HCAPLUS
DN 130:49527
TI Chemistry control in clinical chemistry assays
IN Peddicord, Julie; Kang, Douglas; Clark, Douglas; Puia, Angela
PA Medical Analysis Inc., USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9856719	A2	19981217	WO 98-US10513	19980521
	W: CN, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 97-874383		19970613		

AB Stabilized **compns.** for use in clin. chem. assays are disclosed. The **compn.** is **stable** in the liq. form. The **compn.** minimizes the use of human derived starting materials and uses recombinant thermophilic enzymes as a substitute for native enzymes commonly used in chem. controls. A stock buffer soln. was prepd. from bis Tris propane, protease-free bovine serum albumin, NaCl, protease-free IgG (the IgG is omitted if recombinant thermophilic acid phosphatase is used), .beta.-cyclodextrin, Tween-20, cholesterol, and **water**.

IT **50-81-7**, **Ascorbic** acid, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(base matrix contg.; chem. control in clin. chem. assays)

IT **50-23-7**, Cortisol **68-19-9**, Vitamin B12 **20830-75-5**, Digoxin
RL: ANT (Analyte); ARU (Analytical role, unclassified); ANST (Analytical study)
(chem. control in clin. chem. assays)

IT **50-99-7**, **Glucose**, analysis
RL: ANT (Analyte); ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)
(chem. control in clin. chem. assays)

IT **103-90-2**, Acetaminophen
RL: ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)
(stability of, in liq. chem. control; chem. control in clin. chem. assays)

IT **7585-39-9**, .beta.-Cyclodextrin **64431-96-5**, Bis Tris propane
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(stock buffer soln. contg.; chem. control in clin. chem. assays)

=> D L25 BIB ABS HITRN 2-14

L25 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684

TI Novel **stable** liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9805314	A1	19980212	WO 97-FR1452	19970805
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2751875	A1	19980206	FR 96-9858	19960805
FR 2751875	B1	19981224		
CA 2233924	AA	19980212	CA 97-2233924	19970805
AU 9739451	A1	19980225	AU 97-39451	19970805
EP 858329	A1	19980819	EP 97-936739	19970805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 96-9858 19960805
WO 97-FR1452 19970805

AB Novel **stable** paracetamol **compns**. for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns**. contain a soln. of paracetamol in an **aq**. solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq**. solvent to remove oxygen from the medium. Said **compns**. may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns**. for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **50-70-4**, **Glucitol**, biological studies **50-81-7D**, **Ascorbic** acid, alk. earth metal salts **50-81-7D**, **Ascorbic** acid, derivs. **50-99-7**, **Glucose**, biological studies **56-81-5**, **Glycerol**, biological studies **57-27-2**, Morphine, biological studies **57-48-7**, Levulose, biological studies **57-55-6**, Propylene **glycol**, biological studies **69-65-8**, **Mannitol 87-89-8**, **Inositol 96-27-5**, .alpha.-Thioglycerol **103-90-2**, Paracetamol **134-03-2**, Sodium **ascorbate** **3483-12-3**, Dithiothreitol **6055-06-7**, Morphine hydrochloride trihydrate **10504-35-5D**, D-**Ascorbic** acid, derivs. **25322-68-3**, Peg **62624-30-0D**, **Ascorbic** acid, alkali metal salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol **compns**.)

L25 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:172582 HCAPLUS
DN 126:176681

TI **Stable** cosmetic **compositions** containing surfactants and fatty alcohols
IN Wagner, Julie Ann; Zukowski, Joseph Michael; Robinson, Larry Richard; Deckner, George Endel; Rinaldi, Marie Antoinette; Szymanski, Victoria Claire
PA Procter & Gamble Company, USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9701326	A1	19970116	WO 96-US10940	19960626
	W: AU, CA, CN, CZ, JP, KR, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2225444	AA	19970116	CA 96-2225444	19960626
	AU 9663968	A1	19970130	AU 96-63968	19960626
	EP 835095	A1	19980415	EP 96-923465	19960626
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRAI US 95-673 19950629
US 95-2170 19950811
US 96-647083 19960508
WO 96-US10940 19960626
OS MARPAT 126:176681
AB The present invention relates to leave on, skin care **compns.**, comprising (A) from about 0.001% to about 20% of an active ingredient, (B) from about 1% to about 20% of a **stable**, hydrophobic, structuring agent selected from the group consisting of satd. C16-30 fatty alcs., satd. C16-30 fatty alcs. contg. from about 1-5 mol of ethylene oxide, satd. C16-30 diols, satd. C16-30 monoglycerol ethers, satd. C16-30 hydroxy fatty acids, and **mixts.** thereof, having a m.p. of at least about 45.degree.; and (C) from about 0.05 to about 10% of a hydrophilic surfactant selected from the group consisting of anionic surfactants, cationic surfactants, zwitterionic surfactants, and **mixts.** thereof; and (D) from about 25% to about 98.949% **water.** These **compns.** are useful for delivering a wide variety of active ingredients to the skin. Thus, a moisturizing oil-in-**water** emulsion contained salicylic acid 2, PPG Bu ether 8.00, glycerin 4.00, stearyl alc. 1.5, cetyl alc. 3.00, distearyldimethylammonium chloride 0.1, propylene **glycol** 3.00, Steareth-21 2.0, Steareth-2 1.0, Dimethicone 1.0, cyclomethicone 1.0, disodium EDTA 0.02, and **water** qs 100%.
IT **50-23-7**, Hydrocortisone **60-54-8**, Tetracycline **96-26-4**, Dihydroxyacetone **103-90-2**, Acetaminophen **108-46-3**, 1,3-Benzenediol, biological studies **25322-68-3D**, fatty ethers
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**stable** cosmetic **compns.** contg. surfactants and fatty alcs.)

L25 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:112885 HCAPLUS

DN 126:122499
TI **Stable** isopropylantipyrine preparations
IN Fuchi, Kumiko; Nishii, Hiroyuki; Shimizu, Takashi; Kato, Keiichi
PA Sumitomo Pharma, Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 08325145	A2	19961210	JP 95-152292	19950526

AB The prepns. consist of (1) cores contg. .gtoreq.1 pharmacol. active ingredients those cause **compositional** changes by mixing with isopropylantipyrine (I), (2) a barrier layer as the 1st layer contg. .gtoreq.1 pharmacol. acceptable film-forming agents, (3) the 2nd layer contg. I, and (4) a moistureproofing layer as the 3rd layer contg. **water**-insol. polymers and **water**-sol. polymers. Core tablets contg. acetaminophen 20.2, dextromethorphan-HBr 2.2, methylephedrine-HCl 2.7, dl-chlorpheniramine maleate 0.3, anhyd. caffeine 3.4, Na L-**ascorbate** 22.5, lactose 16.9, cornstarch 7.2, CM-cellulose Ca 2.6, poly(vinylpyrrolidone) 2.0, isopropamide iodide 0.3, and Mg stearate 0.7 part were coated firstly with 1.2 parts hydroxypropyl Me cellulose, secondly with 13.5 parts I and 2.3 parts hydroxypropyl Me cellulose (II), and thirdly with 1.9 parts II and 0.1 part poly(vinyl acetal) diethylaminoacetate (III) to give tablets. The tablets were kept at 50.degree. for 2 wk to show no changes in the contents nor in the appearance, while control tablets without III showed browning and decrease in some of the contents by the similar treatment.

IT **103-90-2**, Acetaminophen **134-03-2**, Sodium L-**ascorbate** **9004-65-3**, Hydroxypropyl methyl cellulose
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** multilayered isopropylantipyrine-contg. prepns. having waterproofing coating layers)

L25 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:926443 HCAPLUS
DN 123:321729
TI Low pH, hydrolytically **stable**, cosmetic **compositions** containing acidic actives
IN Deckner, George Endel; Rinaldi, Marie Antoinette; Szymanski, Victoria Claire
PA Procter and Gamble Co., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9524179	A1	19950914	WO 95-US2840	19950307
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UG, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2185231	AA	19950914	CA 95-2185231	19950307

	AU 9519825	A1	19950925	AU 95-19825	19950307
	EP 748203	A1	19961218	EP 95-912775	19950307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1145582	A	19970319	CN 95-192519	19950307
	JP 09510208	T2	19971014	JP 95-523594	19950307
	US 5824666	A	19981020	US 95-576264	19951221
PRAI	US 94-212413	19940311			
	WO 95-US2840	19950307			

OS MARPAT 123:321729

AB The present invention relates to leave on, oil-in-**water**, skin care **compns**. comprising (1) 0.05-20% of an acidic active ingredient, preferably having a soly. parameter of 6-12; (2) 0.1-25% of alkoxylated alcs., alkoxylated polyols, and **mixts**. thereof; (3) 1-20% of an acid **stable**, hydrophobic structuring agent selected from the group consisting of satd. C16-30 fatty alcs., satd. C16-30 fatty alcs. contg. 1-5 mol of ethylene oxide, satd. C16-30 diols, satd. C16-30 monoglycerol ethers, satd. C16-30 hydroxy fatty acids, and **mixts**. thereof, having a m.p. of .gtoreq.45.degree.; (4) 0.05-10% of an acid **stable**, hydrophilic surfactant selected from the group consisting of anionic, cationic, zwitterionic, nonionic surfactant, and **mixts**. thereof; and (5) 25-99.7% **water**, wherein the pH of the **compn**. is .ltoreq.3.5. These cosmetic **compns**. provide improved phys. and chem. stability, while providing good skin deposition and good skin penetration of the active ingredients, while also providing low dermal irritation. An oil-in-**water** emulsion moisturizer contained salicylic acid 2, PPG-14 Bu ether 8, glycerin 4, stearyl alc. 1.5, cetyl alc. 3, distearyldimethylammonium chloride 0.1, propylene **glycol** 3, steareth-21 2, steareth-2 1, dimethicone 1, cyclomethicone 1, di-Na EDTA 0.02, minor ingredients 0.07, and **water** to 100%.

IT **50-23-7**, Hydrocortisone **56-81-5**, Glycerin, biological studies **57-55-6**, Propylene **glycol**, biological studies **60-54-8**, Tetracycline **96-26-4**, Dihydroxyacetone **103-90-2**, Acetaminophen **108-46-3**, Resorcinol, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** topical **compns**. contg. acidic actives for desquamation and moisturization)

L25 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 1999 ACS

AN 1995:496087 HCAPLUS

DN 122:276434

TI Characterization and investigation of the electrocatalytic properties of poly-p-phenylene modified electrodes

AU Rubinson, Judith F.; Neff, Shellie; Mark,, Harry B. Jr.; Galal, Ahmed; Atta, Nada F.

CS Department of Chemistry, College of Mount St. Joseph, 5701 Delhi Road, Cincinnati, OH, 45233-1670, USA

SO J. Electroanal. Chem. (1995), 384(1-2), 19-23
CODEN: JECHES; ISSN: 0368-1874

DT Journal

LA English

AB Poly-p-phenylene was polymd. electrochem. on the surface of platinum and glassy carbon electrodes. The polymer film differs both in morphol. and in effects of modification when a comparison is made between the modified platinum and modified glassy carbon surfaces. The modified electrodes decrease the overpotential for oxidn. of such biol. important compds. as NADH, acetaminophen, catechol, p-aminophenol, and **ascorbic** acid.

In addn. to the decrease in overpotential, there is also an increase in the current for the oxidative process. The electrodes are **stable** chem. and electrochem. both in **aq.** soln. and in **mixts.** contg. methanol, making them excellent candidates for sensing and/or electrocatalytic applications.

IT **50-81-7, Ascorbic** acid, properties **58-68-4,** NADH **103-90-2,** Acetaminophen **120-80-9,** Catechol, properties
RL: PRP (Properties); RCT (Reactant)
(electrochem. oxidn. and oxidn. potential on poly-p-phenylene-modified glassy carbon or platinum)

L25 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:277191 HCAPLUS
DN 122:38853
TI manufacture of coated compound tablets containing vitamin C, acetaminophen, chlorpheniramine, and Yinqiao extract
IN Yu, Kaifu; Liu, Guosheng; Huang, Ying
PA Shanghai Pharmaceutical Factory, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1082889	A	19940302	CN 93-105579	19930513

AB Compd. tablets are prepd. contg. vitamin C 300-360, Yinqiao ext. 900-1100, , acetaminophen 650-750, chlorpheniramine 6-8, calcium carbonate 90-110, starch 500-600, dextran 100-120, peppermint oil 7-7.5 parts, and Yinqiao and jingfang volatile oils. The tablets are coated with a **compn** . contg. hydroxypropylmethyl cellulose, no. 2 enteric vinyl resin, PEG 6000, sesame oil, Tween 80, titanium oxide, talc, Mg stearate, food color, 95% ethanol, and distd. **water.** The tablets were **stable** and superior to **sugar** coating.

IT **50-81-7,** Vitamin C, biological studies **103-90-2,** Acetaminophen
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(manuf. of coated compd. tablets contg. vitamin C, acetaminophen, chlorpheniramine, and Yinqiao ext.)

L25 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:686631 HCAPLUS
DN 121:286631
TI Taste-masked **aqueous** pharmaceutical suspension and process for preparation thereof
IN Ratnaraj, Sheila M.; Sunshine, Warren L.
PA McNeil-PPC, Inc., USA
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI EP 620001 A1 19941019 EP 94-302700 19940415
R: DE, DK, ES, FR, GB, IT, SE
CA 2121435 AA 19941017 CA 94-2121435 19940415
FI 9401777 A 19941017 FI 94-1777 19940415
NO 9401358 A 19941017 NO 94-1358 19940415
US 5658919 A 19970819 US 96-711140 19960909
PRAI US 93-48701 19930416
US 95-383542 19950203
AB The present invention relates to an **aq**. pharmaceutical suspension **compn**. contg. acetaminophen and at least one addnl. pharmaceutical agent, a suspension system contg. xanthan gum, a **mixt**. of microcryst. cellulose, Na CM-cellulose, and an auxiliary suspending agent selected from the group consisting of hydroxyethyl cellulose and a pharmaceutically acceptable salt of CM cellulose, an effective amt. of a taste-masking sweetener or flavoring agent, and **water**. The suspension is physicochem. **stable** and esp. well suited for both geriatric and pediatric applications. For example, a pediatric cold suspension contained acetaminophen powder 3.2, pseudoephedrine HCl 0.3, chloropheniramine maleate 0.02, **fructose** corn syrup 73.0, purified **water** 20.0, **sorbitol** soln. 20.0, glycerin 10.0, xanthan gum 0.14, CM cellulose 0.56, Na CM cellulose 0.03, butylparaben 0.025, Na benzoate 0.2, propylene **glycol** 0.25, malic acid 0.076, citric acid 0.038, coloring 0.002, and artificial grape flavoring 0.2 g/100 mL.
IT **103-90-2**, Acetaminophen **9004-62-0**, Hydroxyethyl cellulose **50679-08-8**, Terfenadine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(taste-masked **aq**. suspension for cold contg. acetaminophen and addn. drugs)

L25 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1992:113534 HCAPLUS
DN 116:113534
TI Self-emulsifying glasses comprising oleaginous material and a **water** soluble matrix
IN Shively, Merrick L.
PA Research Corp. Technologies, Inc., USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9118613	A1	19911212	WO 91-US3864	19910531
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2059555	AA	19911202	CA 91-2059555	19910531
AU 9182106	A1	19911231	AU 91-82106	19910531
AU 648573	B2	19940428		
EP 489898	A1	19920617	EP 91-912696	19910531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 07501259	T2	19950209	JP 91-511745	19910531
JP 06182189	A2	19940705	JP 92-81184	19920402
JP 06165931	A2	19940614	JP 92-82388	19920403
PRAI US 90-531847		19900601		
WO 91-US3864		19910531		

AB A self-elmulsifying glass comprises a **mixt**. of an oleaginous

material and a non surface active, **water**-sol. matrix; the glass being .apprx.10-60% microcryst. as detd. by differential scanning calorimetry is capable of forming a **stable** emulsion upon contact with a sufficient amt. of an **aq.** phase. The glass and emulsions produced therefrom are useful for pharmaceutical, food and cosmetic applications. Progesterone was dissolved in safflower oil, then **sucrose** was added to the oil before addn. of **water** to dissolve the **sucrose**. The **water** was evapd. to obtain a solid which formed an oil in **water** emulsion when combined with **water**.

IT **50-99-7**, **Glucose**, biological studies **57-48-7**, **Fructose**, biological studies **57-50-1**, **Sucrose**, biological studies **99-20-7**, Trehalose **103-90-2**, Acetaminophen **36894-69-6**, Labetalol
RL: BIOL (Biological study)
(glass matrix comprising, self-emulsifying)

L25 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1989:484130 HCAPLUS
DN 111:84130
TI Syrups containing lysozyme and additional bromhexine using maltitol with improved stability
IN Ogawa, Noriyuki; Tsumori, Katsuyuki; Mizuno, Takahiro
PA Kowa Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63313734	A2	19881221	JP 87-150851	19870617
JP 08019000	B4	19960228		

AB **Stable** syrup **formulations** contain lysozyme (I) or its salt and addnl. bromhexine (II) or its salt as active ingredients, and maltitol (III) as a **sugar**. A soln. of I chloride (IV) 0.6, reduced malt starch **sugar** (contg. 75-80% III) 100, II.HCl 0.12, p-HOC6H4CO2Me (V), p-HOC6H4CO2Et (VI), and p-HOC6H4CO2Pr (VII) in purified **water** was adjusted to pH 4.6 with citric acid and Na citrate to give 300 mL syrup, which was sterilized, filled in brown bottles, and stored at 40.degree. for 6 mo. The syrup remained transparent and the intact IV was 100.0%, but the control with **sucrose** instead of III became brown and the intact IV was 94.3%. A syrup (3000 mL) at pH 4.0 was prepd. which contained IV 6.0, II.HCl 1.2, dihydrocodeine phosphate 3.0, dl-methylephedrine hydrochloride 7.5, chlorpheniramine maleate 1.2, powd. reduced malt starch **sugar** (contg. .gtoreq.93% III) 2000.0, V 0.6, VI 0.9, VII 0.6, citric acid, and Na citrate in purified **water**.

IT **103-90-2**, Acetaminophen
RL: BIOL (Biological study)
(pharmaceutical syrup contg. lysozyme and bromhexine and, maltitol for stabilization of)

IT **585-88-6**, Maltitol
RL: BIOL (Biological study)
(pharmaceutical syrups contg. lysozyme and bromhexine and)

L25 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 1999 ACS

AN 1989:484108 HCAPLUS
DN 111:84108
TI Pharmaceuticals containing spun **sugar** fibers as solid carriers
IN Fuisz, Richard C.
PA USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8808298	A1	19881103	WO 88-US1199	19880414
	W: AU, BR, HU, JP, KR, SU				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4855326	A	19890808	US 88-169838	19880318
	IL 86053	A1	19910916	IL 88-86053	19880413
	AU 8817104	A1	19881202	AU 88-17104	19880414
	AU 609137	B2	19910426		
	EP 357665	A1	19900314	EP 88-904094	19880414
	EP 357665	B1	19940302		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03500164	T2	19910117	JP 88-503773	19880414
	HU 54491	A2	19910328	HU 88-3238	19880414
	HU 207941	B	19930728		
	AT 102021	E	19940315	AT 88-904094	19880414
	RU 2056835	C1	19960327	RU 88-4742414	19880414
	CA 1315679	A1	19930406	CA 88-564394	19880418
	ZA 8802770	A	19881228	ZA 88-2770	19880420
	ZA 8802771	A	19881228	ZA 88-2771	19880420
	WO 9107952	A1	19910613	WO 90-US6093	19901024
	W: AU, BR, HU, JP, KR, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9066488	A1	19910626	AU 90-66488	19901024
	AU 640966	B2	19930909		
	EP 502865	A1	19920916	EP 90-916659	19901024
	EP 502865	B1	19950906		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	BR 9007887	A	19920929	BR 90-7887	19901024
	IL 96199	A1	19941128	IL 90-96199	19901031
	CA 2029175	AA	19910531	CA 90-2029175	19901101
	CA 2029175	C	19960521		
	ZA 9009092	A	19910925	ZA 90-9092	19901113
	CA 2141909	AA	19950811	CA 95-2141909	19950206
	EP 667147	A2	19950816	EP 95-650004	19950208
	EP 667147	A3	19960424		
	R: BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
	JP 08038138	A2	19960213	JP 95-43651	19950209
	CN 1119934	A	19960410	CN 95-102933	19950210

PRAI	US 87-40371	19870420
	US 88-169838	19880318
	EP 88-904094	19880414
	WO 88-US1199	19880414
	US 89-444045	19891130
	WO 90-US6093	19901024
	US 94-194682	19940210

AB A pharmaceutical comprises a mass of spun fibers of a material that is readily **water**-sol. and a pharmacol. active agent distributed throughout the fibrous mass. A slurry contg. 60-70% wt./vol.

acetaminophen and iso-PrOH was mixed with granular **sugar** and the granules were uniformly coated with the slurry, dried for 3-4 h at 45-65.degree., and the dried granules were converted to fibers on a conventional cotton candy machine to give a pediatric **formulation**. The pharmaceutical had the appearance of cotton candy and contained 87.0-91.0% by wt. acetaminophen. The material is compacted preferably to a wafer-like structure while avoiding fracturing the fibers and retaining the fibrous character in order to ensure rapid dissoln. in saliva or in a solvent; the **compn.** is packaged in a moisture-proof package or wrapper. **Sucrose** is susceptible to deterioration in the presence of moisture, however the inclusion of 10% by wt. lactose gives a more **stable** product; lactose absorbs moisture and acts as desiccant. Spinning of a **mixt.** of 10% flavored lactose and **sucrose** at the temp. required for spinning **sucrose** results in a **compn.** wherein the lactose is uniformly dispersed throughout the fibrous mass. Lactose alone is a good carrier, with or without sweetener, and removes the unpleasant aftertaste of the drug.

IT **57-50-1**, biological studies
RL: BIOL (Biological study)
(fiber, as pharmaceutical carriers)

IT **50-70-4**, **Sorbitol**, biological studies **50-99-7**, D-**Glucose**, biological studies **57-48-7**, **Fructose**, biological studies **63-42-3**, Lactose **69-65-8**, **Mannitol 69-79-4**, Maltose
RL: BIOL (Biological study)
(fibers, as pharmaceutical carriers)

IT **103-90-2**, Acetaminophen **2375-03-3**, Methylprednisolone sodium succinate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg., **sugar** fibers as carriers for)

L25 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1987:90094 HCAPLUS
DN 106:90094
TI Optimization of a **formulation** for oral pain relief
AU Fuertig, W.; Gaensicke, H.; Box, A.
CS Zent. Bereichs Med., Wilhelm-Pieck-Univ. Rostock, Rostock, Ger. Dem. Rep.
SO Pharm. Prax. (1986), 41(5), 219-21
CODEN: PHPXAK; ISSN: 0048-3656
DT Journal
LA German
AB From a no. of paracetamol [**103-90-2**]- and codeine phosphate [52-28-8]-contg. oral **formulations** tested, the following **formulation** gave a **stable mixt.**: paracetamol 12, EtOH [64-17-5] (90%) 50.0, Tinct. Aurantii 3.5, codeine phosphate 0.81, sodium saccharin 0.5, **water** 2.5 and **sorbitol** [**50-70-4**] (70%) to 190.0 g. In the absence of light the **formulation** was **stable** for 6 mo. Decreasing the EtOH content form 80.0 g to 50.0 g and increasing the **sorbitol** content improved the taste of the **formulation**. A review on the origin and possibilities of pain treatment and various analgesics used is given.

IT **50-70-4**, biological studies
RL: BIOL (Biological study)
(codeine and paracetamol oral **formulations** contg., for pain relief)

IT **103-90-2**, Paracetamol
RL: BIOL (Biological study)
(oral pain relief **formulation** contg.)

L25 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1986:56415 HCAPLUS
DN 104:56415
TI Dry, **water**-foamable pharmaceutical **compositions**
IN Chavkin, Leonard
PA Health Products Development, Inc., USA
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 153836	A2	19850904	EP 85-301018	19850215
	EP 153836	A3	19861230		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4613497	A	19860923	US 84-584788	19840229
	CA 1238274	A1	19880621	CA 85-475180	19850226
	JP 60222427	A2	19851107	JP 85-40270	19850227
PRAI	US 84-584788		19840229		

AB An anhyd. foamable **compn.** capable of forming a **stable** foam on contact with **H2O** contains a polysaccharide gum, an effervescent base comprising carbonates, and a gelling agent such as Ca **gluconate** and Ca lactate. This foam **compn.** gives an immediate action and a long-life compared to conventional foams. Vaginal contraceptives and gastric antacids can be incorporated into the **compn.** Thus, a vaginal contraceptive **compn.** was **formulated** contg. Na alginate 500, NaHCO3 500, citric acid 500, Ca **gluconate** 200, Nonoxynol 9 100, and lactose 500 mg/dosage unit.
IT **103-90-2 299-28-5**
RL: BIOL (Biological study)
(pharmaceutical **water**-foamable **compn.** contg.)

L25 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 1999 ACS
AN 1985:529087 HCAPLUS
DN 103:129087
TI **Stable** 4-hydroxyacetanilide solutions
IN Zukovics, Jozsef, Mrs.; Hoor, Maria; Toth, Jozsef, Mrs.; Tombor, Janos
PA EGYT Gyogyszervegyeszeti Gyar, Hung.
SO Hung. Teljes, 9 pp.
CODEN: HUXXBU
DT Patent
LA Hungarian
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	HU 34687	O	19850429	HU 83-3450	19831005
	HU 188965	B	19860528		

AB 4-Hydroxyacetanilide (I) [**103-90-2**] solns. are **formulated** with propylene **glycol** [**57-55-6**] and **sorbitol** [**50-70-4**] for enhanced stability. Thus, a soln. contg. I 24, EtOH 96, propylene **glycol** 210, CHCl3 1.473, **sucrose** 225, Aravit Red 0.022, raspberry flavor 0.342, **H2O** 185, and 70% **Sorbitol** 460 g was **stable** for 3 yr, whereas a std. I soln. was **stable** only for 6 mo.
IT **50-70-4**, biological studies **57-55-6**, biological studies
RL: BIOL (Biological study)
(hydroxyacetanilide solns. stabilization by)

IT **103-90-2**
RL: BIOL (Biological study)
(stabilization of solns. of)

=> D BIB ABS HITRN L12

L12 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel stable liquid injectable paracetamol compositions
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805314	A1	19980212	WO 97-FR1452	19970805
	W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2751875	A1	19980206	FR 96-9858	19960805
	FR 2751875	B1	19981224		
	CA 2233924	AA	19980212	CA 97-2233924	19970805
	AU 9739451	A1	19980225	AU 97-39451	19970805
	EP 858329	A1	19980819	EP 97-936739	19970805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FR 96-9858	19960805			
	WO 97-FR1452	19970805			

AB Novel stable paracetamol compns. for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The compns. contain a soln. of paracetamol in an **aq.** solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water** -insol. inert gas is carefully bubbled through the **aq.** solvent to **remove oxygen** from the medium. Said compns. may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable compns. for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel stable liq. injectable paracetamol compns.)

=> D BIB ABS HITRN L17

L17 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:268331 HCAPLUS
DN 128:326507
TI Pharmaceutical **composition** for rapid suspension in **aqueous** media
IN Calanchi, Massimo Maria; Marconi, Marco Giuseppe Raffaele; Mapelli, Luigi Giovanni
PA Eurand International S.P.A., Italy; Calanchi, Massimo Maria; Marconi, Marco Giuseppe Raffaele; Mapelli, Luigi Giovanni
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817250	A1	19980430	WO 97-EP5863	19971023
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	GB 2318511	A1	19980429	GB 96-22090	19961023
	AU 9851887	A1	19980515	AU 98-51887	19971023
PRAI	GB 96-22090		19961023		
	WO 97-EP5863		19971023		

AB The invention provides a granular **compn.** useful as a pharmaceutical carrier which can be used for the prepn. of pharmaceutical **compns.** that are capable of rapid suspension in **water** or **aq.** media including saliva. The **compns.** may be used by addn. to a glass of **water** with stirring or taken directly in the mouth. The granular **compn.** may be prepd. by a process which comprises subjecting a **mixt.** of a thickening agent and a disintegrating agent to wet granulation with an **aq.** medium as wetting agent or dry granulation to make a novel granular product and prepg. the pharmaceutical **compn.** from the granular product and the drug. A **water**-sol. inert excipient, which may be a sugar, may be mixed with the granular product prior to mixing with the drug. Base granules were prepd. contg. Keltrol F, Ac-di-Sol, Avicel PH 200 and Explotab. These granules were mixed with Karion, aspartame and orange flavor and monodose sachets were prepd. from this **mixt.** and **5**-aminosalicylic acid coated with Eudragit S.

IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **compn.** for rapid suspension in **aq.** media)

=> D BIB ABS HITRN L81 1-4

L81 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel **stable** liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9805314	A1	19980212	WO 97-FR1452	19970805
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2751875	A1	19980206	FR 96-9858	19960805
FR 2751875	B1	19981224		
CA 2233924	AA	19980212	CA 97-2233924	19970805
AU 9739451	A1	19980225	AU 97-39451	19970805
EP 858329	A1	19980819	EP 97-936739	19970805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 96-9858 19960805
WO 97-FR1452 19970805

AB Novel **stable** paracetamol **compns**. for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns**. contain a soln. of paracetamol in an **aq**. solvent combined with a **buffer** having a pH of **4** to **8**, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq**. solvent to remove oxygen from the medium. Said **compns**. may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns**. for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = **6**.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol **compns**.)

L81 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 1999 ACS
AN 1993:66861 HCAPLUS
DN 118:66861
TI **Stable** suspension **formulations** for controlled drug delivery
IN Chang, Nienyuan J.
PA Allergan, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent

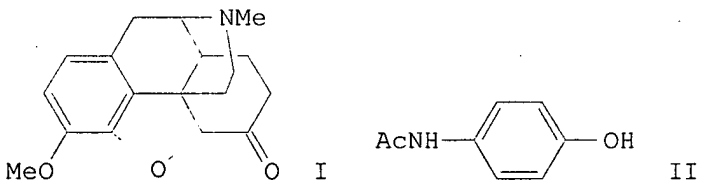
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9211871	A1	19920723	WO 91-US9480	19911217
	W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MW, NO, RO, SD, SU				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	US 5275820	A	19940104	US 90-634500	19901227
	AU 9191306	A1	19920817	AU 91-91306	19911217
	EP 564537	A1	19931013	EP 92-902222	19911217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 06504051	T2	19940512	JP 91-502746	19911217
PRAI	US 90-634500	19901227			
	WO 91-US9480	19911217			

AB Sustained-release pharmaceuticals are prepd. by incorporating small ion-exchange resin particles in microcapsules (prior to incorporation in a polymer matrix) and utilizing these microcapsules in liq. suspensions. The **compns.** have improved drug delivery properties and long-term storage **stability**. Thus, 0.2 g Bio-Rad AG50W-X8 was added to 10 mL **aq.** soln. of levobunolol-HCl and filtered. The drug-bound resin was dried and suspended in 50 mL MeCN soln. of poly(methyl vinyl ether-maleic anhydride) (60%). Sep., 1.5 g poly(vinylpyrrolidone) (mol. wt. 22,000) was dissolved in 25 mL MeCN and the resulting soln. was added to the resin. A white matrix ppt. with resin particles embedded in it was formed. The ppt. was washed with MeCN and dried. The final drug content in the polymer matrix was **8.5**% (by wt.). In pH **7.4 buffer**, a drug release of >**6** h was obsd.

IT **103-90-2**
RL: BIOL (Biological study)
(sustained-release suspension for, polymers and ion exchangers in)

L81 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 1999 ACS
AN 1982:623068 HCAPLUS
DN 97:223068
TI Simultaneous assay of hydrocodone bitartrate and acetaminophen in a tablet **formulation**
AU Wallo, Warren E.; D'Adamo, Anthony
CS Anal. Res. Dep., Knoll Pharm. Co., Whippany, NJ, 07981, USA
SO J. Pharm. Sci. (1982), 71(10), 1115-18
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
GI



I II

AB hydrocodone (I) [125-29-1] and acetaminophen (II) [**103-90-2**] were simultaneously detd. in tablets by reversed-phase high-pressure liq. chromatog. The sepn. method was based on an octadecylsilane column with a **buffered** (pH **4.5**) MeOH-**H2O** mobile phase. Measurement was with a UV spectrophotometer set at 283 nm, compared to external stds. Assays for the active ingredients in tablet samples averaged 99.7% of the label claim for I bitartrate and 100.3% for II. The resp. relative std. deviations of the retention time and precision were 2.2 and 1.75% for I and 3.3 and 0.95% for II. The range of interest studied was 0.035 to 0.065 mg/mL for I bitartrate and 3.50 to **6**.50 mg/mL for II. The assay method was also compared to colorimetric and USP procedures for the active ingredients. The method was suitable for control, content uniformity, and **stability** -indicating use.

IT **103-90-2**
RL: ANST (Analytical study)
(simultaneous detn. of hydrocodone and, in tablets by high-pressure liq. chromatog.)

L81 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 1999 ACS
AN 1979:142154 HCAPLUS
DN 90:142154
TI **Stable** analgesic, antipyretic and antitussive pharmaceuticals
IN Takase, Muneaki; Tago, Kenzo
PA Zenyaku Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 54005022	A2	19790116	JP 77-70363	19770614
JP 55047609	B4	19801201		

AB **Stable** analgesic, antipyretic and antitussive pharmaceuticals are prepd. by mixing **aq**. Glycyrrhiza glabra exts. and acetaminophen [**103-90-2**] with Na citrate [68-04-2] or the **buffers** KH2PO4-K2HPO4 or NaH2PO4-Na2HPO4 and adjusting pH to **5**.0-**6**.5. Thus, distd. **H2O** (150 mL), G. glabra ext. (3.0 g), acetaminophen (3.0 g) and sucrose (100 g) were mixed, heated and filtered. The filtrate was then mixed with Na citrate (1.0 g) and distd. **H2O** to 250 mL. The **compn**. showed synergistic effects. Almost no change was noted after standing at room temp. for 1 mo.

IT **103-90-2**
RL: BIOL (Biological study)
(**stable** pharmaceuticals contg. Glycyrrhiza ext. and and sodium citrate and)

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=> d his

     (FILE 'HOME' ENTERED AT 07:05:59 ON 01 MAR 1999)

     FILE 'REGISTRY' ENTERED AT 07:07:44 ON 01 MAR 1999
L1            1 S PARACETAMOL/CN

     FILE 'MEDLINE, BIOSIS, EMBASE, CEN, DRUGB, DRUGNL, JICST-EPLUS, LIFESCI,
     SCISEARCH, WPIDS' ENTERED AT 07:09:03 ON 01 MAR 1999

     FILE 'REGISTRY' ENTERED AT 07:09:13 ON 01 MAR 1999
               SET SMARTSELECT ON
L2          SEL L1 1- CHEM :      83 TERMS
               SET SMARTSELECT OFF

     FILE 'MEDLINE, BIOSIS, EMBASE, CEN, DRUGB, DRUGNL, JICST-EPLUS, LIFESCI,
     SCISEARCH, WPIDS' ENTERED AT 07:09:15 ON 01 MAR 1999
L3         49089 S L2
L4         49089 S PARACETAMOL OR L3
L5          2027 S L4 AND (AQUEOUS OR WATER OR H2O)
L6           160 S L5 AND (POLYHYDRIC OR INOSITOL OR SORBIT? OR GLYCEROL OR SUG
L7           308 S L5 AND (SUCROSE OR FRUCTOSE OR ASCORB? OR GLUC? )
L8             0 S L5 AND (PROPANE DIOL OR DIHYDROXYPROPANE)
L9           432 S L6 OR L7
L10            0 S L9 AND (BUBBL?)
L11           30 S L9 AND BUFFER?
L12           60 S PARACETAMOL(20A)BUFFER?
L13            3 S L12 AND L9
L14            0 S L9 AND FREE RADICAL(9A)SCAVANG?
L15          242 S L5 AND (SUCROSE OR FRUCTOSE OR GLUC? )
L16          368 S L6 OR L8 OR L15
L17            0 S L16 AND ASCORB? AND FREE RADICAL
L18           35 S L16 AND ASCORB?
L19            3 S L16 AND ASCORB?(9A)PARACETAMOL
L20            3 DUP REMOV L19 (0 DUPLICATES REMOVED)
L21            3 S L16 AND ASCORB?(19A)PARACETAMOL
L22           50 S L16 AND (THIO? OR MERCAPT? OR CYSTEIN? OR ETHANESULFON? OR T
L23           10 S L16 AND (ACETYLCYST? OR MERCAPTOETHANE?)
L24           57 S L22 OR L23
L25            0 S L16 AND (ACETYLCYST? OR MERCAPTOETHANE?)(20A)PARACETAMOL
L26            0 S L16 AND (ACETYLCYST? OR MERCAPTOETHANE?)(30A)PARACETAMOL
L27           13 S L16 AND (THIO? OR MERCAPT? OR CYSTEIN? OR ETHANESULFON? OR T
L28            6 DUP REMOV L27 (7 DUPLICATES REMOVED)
L29            0 S L16 AND (DITHIOTHREIT? OR REDUCED?(3A)GLUTATHION OR ETHANESU
L30            0 S L16 AND ISOTONIZ?
L31            2 S L16 AND STERLI?
L32            0 S L16 AND (CNS OR CENTRAL NERVOUS)(9A)ANALGES?
L33           11 S L16 AND (MORPHIN?)
L34           27 S L16 AND (COMPLEX? OR CHELAT?)
L35            3 S L34 AND STABL?
L36            1 S L16 AND (COMPLEX? OR CHELAT?)(20A)PARACETAMOL
L37            4 S L35 OR L36
L38            7 DUP REMOV L33 (4 DUPLICATES REMOVED)
L39            0 S L16 AND (PHENYLPIPERIDIN? OR NIPECOTIC OR PHENYLCYCLOHEXANOL
L40            0 S L16 AND PHENYLAZEPINE
L41           14 S L16 AND (ANTIINFLAM? OR ANTI INFLAM? OR NSAI? OR KETOPROF?)
L42           14 S L16 AND (IBUPROFEN OR FENOPROFEN OR FLURIBIPROFEN?)
L43           24 S L41 OR L42
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L44          2 S L43 AND STABL?
L45          4 S L43 AND KETOPROF?
L46          0 S L16 AND (ANTIMETIC OR DIMENHYDRIN OR DIPHENIDOL )
L47          2 S L16 AND (GRANISETRON OR MECLIZINE OR ONDANSETRON)
L48          3 S L16 AND (PROCHLORPERAZ? OR PROMETHAZIN? OR SCOPOLAMINE?)
L49          0 S L16 AND (THIETHYLPERAZINE OR TRIMETHOBENZAMID?)
L50          4 S L46-L49
L51          4 DUP REMOV L50 (0 DUPLICATES REMOVED)
L52          5 S L16 AND (ANTIEPILEP? OR CARBAMAZ? OR DIVALPRO? OR FELBAMATE?
L53         13 S L16 AND (GABAPENTIN OR PHENOBARBITAL OR PHENYLTROIN)
L54          1 S L16 AND (PHENSUXIMIDE OR VALPROIC)
L55         19 S L52-L54
L56         19 S L52 OR L53 OR L54
L57          0 S L52 AND STABL?
L58          0 S L53 AND STABL?
L59          0 S L54 AND STABL?
L60         12 S L16 AND (CORTICOSTEROID? OR HYDROCORTIS?)
L61          0 S L16 AND  TRICYCLIC ANTIDEPRESS?
L62          5 S L16 AND (AMITRIPTYL? OR CLOMIPRAMIN? OR DOXEPIN)
L63          1 S L16 AND (IMIPRAMINE OR TRIMIPRAMINE)
L64          1 S L16 AND (AMOXAPINE OR DESIPRAMINE OR NORTRIPTYLINE OR PROTRI
L65          6 S L62 OR L63 OR L64

=> d l13 1-3 bib abs


L13  ANSWER 1 OF 3  EMBASE  COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN   87025256  EMBASE
DN   1987025256
TI   High-performance liquid chromatography systems for the analysis of
     analgesic and non-steroidal anti-inflammatory drugs in forensic
     toxicology.
AU   Stevens H.M.; Gill R.
CS   Central Research Establishment, Home Office Forensic Science Service,
     Reading, Berkshire, RG7 4PN, United Kingdom
SO   Journal of Chromatography, (1986) 370/1 (39-47).
     CODEN: JOCRAM
CY   Netherlands
DT   Journal
FS   037     Drug Literature Index
     029     Clinical Biochemistry
     052     Toxicology
     049     Forensic Science Abstracts
LA   English
AB   High-performance liquid chromatography retension data are presented for
     over 40 analgesic drugs on an ODS-silica packing material to assist in
the
     identification of these compounds. Three isocratic eluents prepared from
     isopropanol, formic acid and an aqueous phosphate buffer
     have been used. One eluent has been used for the analysis of
     paracetamol in whole blood.

L13  ANSWER 2 OF 3  SCISEARCH  COPYRIGHT 1999 ISI (R)
AN   1998:194666  SCISEARCH
GA   The Genuine Article (R) Number: YZ716
TI   Electrochemical poly(1,3-phenylenediamine) synthesis as enzyme
     immobilization media
AU   Ekinci E; Ogunc S T; Karagozler A E (Reprint)
CS   INONU UNIV, FAC ARTS & SCI, DEPT CHEM, TR-44069 MALATYA, TURKEY
(Reprint);
```

INONU UNIV, FAC ARTS & SCI, DEPT CHEM, TR-44069 MALATYA, TURKEY
CYA TURKEY
SO JOURNAL OF APPLIED POLYMER SCIENCE, (4 APR 1998) Vol. 68, No. 1, pp. 145-152.
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0021-8995.
DT Article; Journal
FS PHYS; ENGI
LA English
REC Reference Count: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Electrochemical polymerization of the 1,3-phenylenediamine in the presence of **glucose** oxidase with KCl **aqueous** electrolyte at a potential of 0.800 V versus Ag-AgCl produces adherent poly(1,3-phenylenediamine) containing enzyme (**glucose** oxidase) film on a platinum electrode. Polymeric sensor prepared in this one-step procedure can be used to determine hydrogen peroxide formed as the result of the enzymatic reaction between **glucose** and **glucose** oxidase in the presence of O-2. The amperometric responses of the resultant enzyme electrode to **glucose** were rapid, reaching steady-state values within 4-5 s, and there was a linear relationship between **glucose** concentration and obtained current up to 6 mM. Polymeric sensor was stable for more 3 months. The **glucose** selectivity of enzyme electrode was determined in the presence of some interfering substances, such as lactose, **sucrose**, urea, uric acid, **paracetamol**, and **ascorbic** acid. Also, the effects of **buffer** concentration, storage conditions, and temperature on the steady-state amperometric responses were studied. Moreover, the Arrhenius activation energy for the enzymatic reaction was calculated. (C) 1998 John Wiley & Sons, Inc.

L13 ANSWER 3 OF 3 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 94-150904 [18] WPIDS
DNC C94-069323
TI Prepn of drug pellets of very even quality - using a granulating liq contg a selective anti-adhesion agent e.g. poly sorbate.
DC A96 B07
IN HELLEN, L; HUSSON, I; KRISTOFFERSSON, E; YLIRUUSI, J
PA (HELL-I) HELLEN L; (HUSS-I) HUSSON I; (KRIS-I) KRISTOFFERSSON E; (YLIR-I) YLIRUUSI J
CYC 48
PI WO 9408567 A1 940428 (9418)* EN 13 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US UZ VN
FI 9204590 A 940410 (9424)
ZA 9307483 A 940629 (9428) 14 pp
AU 9351129 A 940509 (9432)
EP 662823 A1 950719 (9533) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
NO 9501370 A 950608 (9534)
JP 08502675 W 960326 (9644) 17 pp
US 5709885 A 980120 (9810) 4 pp
FI 101039 B1 980415 (9821)
ADT WO 9408567 A1 WO 93-FI409 931008; FI 9204590 A FI 92-4590 921009; ZA 9307483 A ZA 93-7483 931008; AU 9351129 A AU 93-51129 931008; EP 662823 A1

EP 93-921946 931008, WO 93-FI409 931008; NO 9501370 A WO 93-FI409 931008, NO 95-1370 950407; JP 08502675 W WO 93-FI409 931008, JP 94-509674 931008; US 5709885 A WO 93-FI409 931008, US 95-411804 950731; FI 101039 B1 FI 92-4590 921009

FDT AU 9351129 A Based on WO 9408567; EP 662823 A1 Based on WO 9408567; JP 08502675 W Based on WO 9408567; US 5709885 A Based on WO 9408567; FI 101039 B1 Previous Publ. FI 9204590

PRAI FI 92-4590 921009

AN 94-150904 [18] WPIDS

AB WO 9408567 A UPAB: 940921

Prepn. of drug pellets comprises: (a) granulating a drug-contg. powder in a rotor-type granulator, by exerting a centrifugal force on the powder in the rotor and bringing it, at or adjacent to the periphery of the rotor, into contact with a granulating liq. which is fed separately into the rotor and converted into a mist in the rotor; (b) extruding the granulate;

and (c) spheroidising the extrudate into pellets which are then dried and opt. coated. The granulating liq. contains a selective anti-adhesion agent

in an amt. of 0.001-5 wt.% of the liq.

The amt. of anti-adhesion agent is 0.01-0.1 wt.% of the granulating liq. The anti-adhesion agent is a polyol (esp. **glycerol** or polyethylene **glycol**) a surfactant (esp. polysorbate or dioctyl sodium sulphosuccinate) or a silicone deriv. The granulating liq. is **water** or a lower alcohol which opt. contains a **buffer**.

The amt. of granulating liq. is 20-100 wt.% of the powder wt. The drug is diltiazem, ibuprofen, **paracetamol** or theophylline.

The powder consists of drug and filler (esp. microcrystalline cellulose). The amt. of filler is at least 30 (esp. 5-20) wt.% of the powder mixt.

USE/ADVANTAGE - Used for prepn. of drug pellets of very even quality.

Process gives drug pellets which exhibit optimal formulation characteristics, such as flow, binding and solubility characteristics.

Dwg.0/0

Dwg.0/0

ABEQ US 5709885 A UPAB: 980309

Prepn. of drug pellets comprises: (a) granulating a drug-contg. powder in a rotor-type granulator, by exerting a centrifugal force on the powder in the rotor and bringing it, at or adjacent to the periphery of the rotor, into contact with a granulating liq. which is fed separately into the rotor and converted into a mist in the rotor; (b) extruding the granulate;

and (c) spheroidising the extrudate into pellets which are then dried and opt. coated. The granulating liq. contains a selective anti-adhesion agent

in an amt. of 0.001-5 wt.% of the liq.

The amt. of anti-adhesion agent is 0.01-0.1 wt.% of the granulating liq. The anti-adhesion agent is a polyol (esp. **glycerol** or polyethylene **glycol**) a surfactant (esp. polysorbate or dioctyl sodium sulphosuccinate) or a silicone deriv. The granulating liq. is **water** or a lower alcohol which opt. contains a **buffer**.

The amt. of granulating liq. is 20-100 wt.% of the powder wt. The drug is diltiazem, ibuprofen, **paracetamol** or theophylline.

The powder consists of drug and filler (esp. microcrystalline cellulose). The amt. of filler is at least 30 (esp. 5-20) wt.% of the powder mixt.

USE/ADVANTAGE - Used for prepn. of drug pellets of very even quality.

Process gives drug pellets which exhibit optimal formulation characteristics, such as flow, binding and solubility characteristics.
Dwg.0/0

=> D BIB ABS HITRN L34

L34 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:301092 HCAPLUS
DN 128:286352
TI Ready-to-use **aqueous** or **water**-alcohol gel with controlled viscosity
PA Barrau, Francois, Fr.
SO Fr. Demande, 15 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2753097	A1	19980313	FR 96-11061	19960911

AB A pharmaceutical , cosmetic, dietetic, or hygienic solid dosage form which is ready to use is disclosed. An effervescent tablet contained paracetamol 500, anhyd. citric acid 1250, sodium bicarbonate 1500, CM-cellulose 300, polyvinyl pyrrolidone 10, magnesium stearate 1, sodium saccharinate 15, and orange flavor 10 mg. After dissoln. of the tablet in a glass of **water** a clear syrupy soln. is obtained.
IT **50-81-7**, **Ascorbic** acid, biological studies **87-69-4**, Tartaric acid, biological studies **103-90-2**, Paracetamol **9004-62-0**, Hydroxyethyl cellulose **9004-64-2** , Hydroxypropyl cellulose **9004-65-3**, Hydroxypropylmethyl cellulose **18472-51-0**, Chlorhexidine gluconate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ready-to-use **aq**. or **water**-alc. gel with controlled viscosity)

=> D BIB ABS HITRN L34 2-11

L34 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:293427 HCAPLUS
DN 129:8597
TI Embedding and encapsulation of controlled release particles
IN Van Lengerich, Bernhard H.
PA Van Lengerich, Bernhard H., USA
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9818610	A1	19980507	WO 97-US18984	19971027
W: AU, CA, JP, NO, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9749915	A1	19980522	AU 97-49915	19971027

PRAI US 96-29038 19961028
US 97-52717 19970716
WO 97-US18984 19971027

AB Controlled release, discrete, solid particles which contain an

encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high **water** binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as **water**, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temp. of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixt. The mixt. is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of **acetylcysteine** is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

IT **50-02-2**, Dexamethasone **50-23-7**, Hydrocortisone **50-24-8**, Prednisolone **50-27-1**, Estriol **50-28-2**, Estradiol, biological studies **50-58-8**, Phendimetrazine tartrate **50-81-7**, **Ascorbic** acid, biological studies **50-96-4**, Isoetharine hydrochloride **51-30-9**, Isoproterenol hydrochloride **51-43-4**, Epinephrine **53-03-2**, Prednisone **56-53-1**, Diethylstilbestrol **56-75-7**, Chloramphenicol **57-22-7**, Vincristine **57-63-6**, Ethinyl estradiol **57-92-1**, Streptomycin, biological studies **58-00-4**, Apomorphine **58-32-2**, Dipyridamole **58-56-0**, Pyridoxine hydrochloride **59-92-7**, Levodopa, biological studies **60-54-8**, Tetracycline **61-76-7**, Phenylephrine hydrochloride **62-31-7**, Dopamine hydrochloride **62-67-9**, Nalorphine **64-31-3**, Morphine sulfate **64-72-2**, Chlortetracycline hydrochloride **66-76-2**, Dicoumarol **67-73-2**, Fluocinolone acetonide **68-19-9**, Cyanocobalamin **71-63-6**, Digitoxin **76-43-7**, Fluoxymesterone **77-09-8** **79-57-2**, Oxytetracycline **80-53-5**, Terpin **81-13-0**, Dexpanthenol **83-43-2**, Methylprednisolone **83-88-5**, Riboflavin, biological studies **84-17-3**, Dienestrol **93-14-1**, Guaifenesin **103-90-2**, Acetaminophen **108-46-3**, Resorcinol, biological studies **114-07-8**, Erythromycin **115-77-5**, Pentaerythritol, biological studies **123-31-9**, Hydroquinone, biological studies **124-94-7**, Triamcinolone **125-72-4**, Levorphanol tartrate **127-33-3**, Demeclocycline **128-46-1**, Dihydrostreptomycin **134-03-2**, Sodium **ascorbate** **136-77-6**, Hexylresorcinol **143-71-5**, Hydrocodone bitartrate **152-97-6**, Fluocortolone **299-27-4**, Potassium gluconate **299-29-6**, Ferrous gluconate **304-59-6**, Potassium sodium tartrate **329-65-7**, 1,2-Benzenediol, 4-[1-hydroxy-2-(methylamino)ethyl]- **357-07-3**, Oxymorphone hydrochloride **378-44-9**, Betamethasone **379-79-3**,

Ergotamine tartrate **382-67-2**, Desoximetasone **426-13-1**, Fluorometholone **434-07-1**, Oxymetholone **437-74-1**, Xantinol nicotinate **465-65-6**, Naloxone **479-18-5**, Dyphylline **514-36-3**, Fludrocortisone acetate **518-47-8**, Fluorescein sodium **527-07-1**, Sodium gluconate **536-21-0** , Norfenefrine **555-30-6**, Methyldopa **564-25-0**, Doxycycline **579-56-6**, Isoxsuprine hydrochloride **652-67-5** , Isosorbide **709-55-7**, Etilefrine **745-65-3**, Alprostadil **859-18-7**, Lincomycin hydrochloride **865-21-4** , Vinblastine **1070-11-7**, Ethambutol hydrochloride **1098-97-1**, Pyritinol **1143-38-0**, Anthralin **1247-42-3**, Meprednisone **1263-89-4**, Paromomycin sulfate **1393-48-2**, **Thiostrepton** **1404-93-9**, Vancomycin hydrochloride **1476-53-5**, Novobiocin sodium **1524-88-5**, Flurandrenolide **1597-82-6**, Paramethasone acetate **2013-58-3**, Meclocycline **2589-47-1**, Prajmalium bitartrate **2589-47-1**, Prajmalium bitartrate, biological studies **3385-03-3**, Flunisolide **3546-41-6**, Pyrvinium pamoate **3632-91-5**, Magnesium gluconate **3963-95-9**, Methacycline hydrochloride **4330-99-8**, Trimeprazine tartrate **4468-02-4** , Zinc gluconate **5355-48-6** **5536-17-4**, Vidarabine **5874-97-5**, Metaproterenol sulfate **6284-40-8**, Meglumine **7054-25-3**, Quinidine gluconate **7681-93-8**, Natamycin **10246-75-0**, Hydroxyzine pamoate **12650-69-0**, Mupirocin **13292-46-1**, Rifampin **13392-18-2**, Fenoterol **13422-51-0**, Hydroxocobalamin **13614-98-7**, Minocycline hydrochloride **18378-89-7**, Plicamycin **18559-94-9**, Salbutamol **19356-17-3**, Calcifediol **20830-75-5**, Digoxin **21462-39-5**, Clindamycin hydrochloride **22204-24-6**, Pyrantel pamoate **23031-25-6**, Terbutaline **23031-32-5**, Terbutaline sulfate **23214-92-8**, Doxorubicin **23288-49-5** , Probucol **23869-24-1**, O-(.beta.-Hydroxyethyl)-rutoside **24390-14-5**, Doxycycline hyclate **24729-96-2**, Clindamycin phosphate **25322-68-3**, Polyethylene glycol **25389-94-0**, Kanamycin sulfate **26652-09-5**, Ritodrine **27823-62-7**, Chlortetracycline bisulfate **28860-95-9**, Carbidopa **30685-43-9**, Metildigoxin **32780-64-6**, Labetalol hydrochloride **33402-03-8**, Metaraminol bitartrate **33419-42-0**, Etoposide **36688-78-5** **36791-04-5**, Ribavirin **37517-28-5**, Amikacin **42200-33-9**, Nadolol **49745-95-1**, Dobutamine hydrochloride **50679-08-8**, Terfenadine **56392-17-7**, Metoprolol tartrate **58551-69-2** , Carboprost tromethamine **60166-93-0**, Iopamidol **60833-22-9**, Pyridoxal 5'-phosphate glutamate **66108-95-0**, Iohexol **81103-11-9**, Clarithromycin **83905-01-5**, Azithromycin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

L34 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:123996 HCAPLUS
DN 128:184696
TI Easy to swallow oral medicament composition
IN Gruber, Peter
PA Losan Pharma G.m.b.H., Germany; Gruber, Peter
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806385	A1	19980219	WO 97-CH299	19970814
	W: AU, BG, BR, CA, CN, CZ, HU, JP, NO, PL, RO, RU, SI, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9736912	A1	19980306	AU 97-36912	19970814
PRAI	CH 96-2006		19960815		
	WO 97-CH299		19970814		

AB An easy-to-swallow pharmaceutical compn. consists of .gtoreq.1 coated particles with a core which contains an active substance and a coat with .gtoreq.1 layers. The coating layer(s) contains .gtoreq.1 hydratable, pharmaceutically acceptable polymer which, on contact with saliva or **water**, forms a coherent, moldable, viscous mass with a slippery surface which does not adhere to the mucous membranes of the mouth, and which prevents the active substance-contg. particles from leaving the mass and releasing the active substance in the mouth cavity. The (outermost) coating layer contains .gtoreq.1 salivation-promoting agent. The properties of the coating make the compn. suitable for administering highly dosed or bad-tasting active substances and even for swallowing without any liq. Thus, a soln. of ciprofloxacin 2000, Crospovidone XL-M 110, PVP K90 60, **water** 900, and EtOH 1800 g was spray-coated onto sucrose crystals 0.3-0.6 mm in diam. to produce core particles, which were then coated first with a powd. mixt. of NaCl 50, Na saccharin 50, and Na carboxymethylstarch 50 g, and finally [after moistening with EtOH-**H2O** (1:1)] with a powd. mixt. of Na CM-cellulose 275 and talc 75 g.

IT **9004-62-0**, Hydroxyethylcellulose **9004-64-2**, Hydroxypropylcellulose **9004-65-3**, Hydroxypropylmethylcellulose **39421-75-5**, Hydroxypropyl guar gum
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coating, hydration of; easy-to-swallow oral medicament compn.)

IT **57-27-2**, Morphine, biological studies **60-54-8**, Tetracycline **103-90-2**, Paracetamol **114-07-8**, Erythromycin **4618-18-2**, Lactulose **15722-48-2**, Olsalazine **50679-08-8**, Terfenadine **51333-22-3**, Budesonide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(easy-to-swallow oral medicament compn.)

IT **50-70-4**, Sorbitol, biological studies **50-81-7**, L-**Ascorbic** acid, biological studies **50-99-7**, D-Glucose, biological studies **57-48-7**, D-Fructose, biological studies **57-50-1**, Sucrose, biological studies **69-65-8**, D-Mannitol **87-69-4**, Tartaric acid, biological studies **87-99-0**, Xylitol **134-03-2**, Sodium **ascorbate 585-88-6**, Maltitol **14475-11-7 15421-15-5**, Potassium **ascorbate 40968-90-9**, Potassium tartrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(easy-to-swallow oral medicament compn.)

L34 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS

DN 128:184684
TI Novel stable liquid injectable paracetamol compositions
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805314	A1	19980212	WO 97-FR1452	19970805
	W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2751875	A1	19980206	FR 96-9858	19960805
	FR 2751875	B1	19981224		
	CA 2233924	AA	19980212	CA 97-2233924	19970805
	AU 9739451	A1	19980225	AU 97-39451	19970805
	EP 858329	A1	19980819	EP 97-936739	19970805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 96-9858 19960805
WO 97-FR1452 19970805

AB Novel stable paracetamol compns. for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The compns. contain a soln. of paracetamol in an **aq**. solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water** -insol. inert gas is carefully bubbled through the **aq**. solvent to remove oxygen from the medium. Said compns. may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable compns. for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **50-70-4**, Glucitol, biological studies **50-81-7D**, **Ascorbic** acid, alk. earth metal salts **50-81-7D**, **Ascorbic** acid, derivs. **50-99-7**, Glucose, biological studies **56-81-5**, Glycerol, biological studies **57-27-2**, Morphine, biological studies **57-48-7**, Levulose, biological studies **57-55-6**, Propylene glycol, biological studies **69-65-8**, Mannitol **87-89-8**, Inositol **96-27-5**, .alpha.-**Thioglycerol 103-90-2**, Paracetamol **134-03-2**, Sodium **ascorbate 3483-12-3**, **Dithiothreitol 6055-06-7**, Morphine hydrochloride trihydrate **10504-35-5D**, D-**Ascorbic** acid, derivs. **25322-68-3**, Peg **62624-30-0D**, **Ascorbic** acid, alkali metal salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel stable liq. injectable paracetamol compns.)

L34 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:440833 HCAPLUS
DN 125:96096
TI Orally applicable pharmaceutical composition containing a **water**

-soluble amino acid as a disintegration accelerator
IN Gajdos, Benedikt; Duerr, Manfred
PA Rhone-Poulenc Rorer Gmbh, Germany
SO Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 715857	A2	19960612	EP 95-118095	19951117
EP 715857	A3	19970528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 4444051	A1	19960613	DE 94-4444051	19941210
AU 9537945	A1	19960620	AU 95-37945	19951120
AU 697187	B2	19981001		
JP 08208520	A2	19960813	JP 95-312613	19951130
CA 2164777	AA	19960611	CA 95-2164777	19951208
ZA 9510427	A	19960618	ZA 95-10427	19951208

PRAI DE 94-4444051 19941210
AB A solid oral dosage form which is mech. strong and resistant to damage, but disintegrates rapidly in the mouth on exposure to **water** or saliva, contains a disintegrating agent and a **water**-sol. amino acid (or salt or deriv. thereof) as disintegration accelerator. These 2 components evidently act synergistically. Thus, a mixt. of ketoprofen 50 and ethylcellulose (disintegrating agent) 5 g was granulated with **H2O**, combined with glycine 119, Polyplasdone XL 10, SiO2 1, flavoring 10, NaCl 1, sweetener 2, and Mg stearate 2 g, and compressed into 200-mg tablets which had a disintegration time of 8-15 s.
IT **50-81-7**, **Ascorbic** acid, biological studies
58-56-0, Pyridoxine hydrochloride **83-88-5**, Riboflavin, biological studies **103-90-2**, Paracetamol **103-90-2D**, Paracetamol, derivs. **64519-82-0**, Palatinit
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical compn. contg. **water**-sol. amino acid as disintegration accelerator)
IT **9004-65-3**, Hydroxypropylmethylcellulose
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical compn. contg. **water**-sol. amino acid as disintegration accelerator)

L34 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1992:484720 HCAPLUS
DN 117:84720
TI Electrophilicity as measured by Ke: molecular determinants, relationship with other physical-chemical and quantum mechanical parameters, and ability to predict rodent carcinogenicity
AU Benigni, R.; Cotta-Ramusino, M.; Andreoli, C.; Giuliani, A.
CS Lab. Comp. Toxicol. Ectoxicol., Ist. Super. Sanita, Rome, Italy
SO Carcinogenesis (London) (1992), 13(4), 547-53
CODEN: CRNGDP; ISSN: 0143-3334
DT Journal
LA English
AB This paper analyzes electrophilicity data as measured by the Ke system for
205 chems. including both rodent carcinogens and non-carcinogens. Multivariate statistical methods were used. The anal. identified atoms

and substructures contributing to electrophilicity, and permitted to establish a theor. method by which the Ke value (electrophilicity) of chems. can be easily estd. In a subset of chems., the Ke parameter was compared with other phys.-chem. and quantum mech. properties: Ke appeared to be mostly correlated with the energy of the LUMO and with the abs. electronegativity. The role of Ke in structure-activity studies was also investigated; in particular, a comparative anal. of the performance of Ke, Salmonella typhimurium and Ashby's structural alerts in predicting carcinogenicity was carried out. The Ke system performed better than the other systems. However, because of the many different mechanisms underlying carcinogenesis, the Ke system cannot predict the potential carcinogenicity of all kinds of chems. It is concluded that the main role of Ke in risk assessment consists in producing a probabilistic est. of the rodent carcinogenicity of the chems.: e.g. a chem. with Ke higher than 3.0 .times. 1012 M-1 s-1 has nearly 80% probability of being a carcinogen. Such a probability est. can be used to rank the chems. in a priority scale for subsequent and more detailed studies, either theor. or exptl. In view of this, the role of the authors' method for estg. Ke is particularly important: it gives rapidly and at no cost a chem. classification for risk assessment and priority setting.

IT **50-81-7**, L-**Ascorbic** acid, biological studies
56-53-1, Diethylstilbestrol **57-55-6**, 1,2-Propanediol, biological studies **57-63-6**, Ethynylestradiol **103-90-2**, Acetaminophen **107-21-1**, 1,2-Ethanediol, biological studies **108-46-3**, QResorcinol, biological studies **121-79-9**, Propyl gallate **458-37-7**, Curcumin **6441-77-6**, Phloxine **16423-68-0**, Erythrosin **17924-92-4**, Zearalenone **33229-34-4**
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(carcinogenicity in rodents of, prediction of, electrophilicity and mol. determinants and quantum mechanics in)

L34 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1991:614862 HCAPLUS
DN 115:214862
TI Uncoated pharmaceutical effervescent tablet
IN Gergely, Gerhard; Gergely, Thomas; Gergely, Irmgard
PA Austria
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9107174	A1	19910530	WO 90-EP1880	19901109
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5064656	A	19911112	US 90-574585	19900828
	EP 501985	A1	19920909	EP 90-916467	19901109
	EP 501985	B1	19940126		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

JP 05501413	T2	19930318	JP 90-515332	19901109
AT 100708	E	19940215	AT 90-916467	19901109
CA 2068714	C	19970422	CA 90-2068714	19901109

PRAI CH 89-4098 19891114
US 90-574585 19900828
EP 90-916467 19901109
WO 90-EP1880 19901109

AB The title tablet contains a pharmaceutical, a disintegrant, a constituent which eliminates a gas on reaction with another tablet constituent, in a wt. ratio of disintegrant to the all other ingredients of (0.1-4.0):1.0. A no. of tablets were prepd. by combining components selected from disintegrants (polyvinylpyrrolidone, starch), effervescent agents (NaHCO3, tartaric acid, fumaric acid, adipic acid, citric acid), and filler (lactose). The tablets disintegrate in **water** rapidly and produce effervescence.

IT **25322-68-3**
RL: USES (Uses)
(gas-generating particle coating with, in effervescent tablet prepn.)

IT **50-81-7**, L-**Ascorbic** acid, biological studies
103-90-2, Paracetamol
RL: BIOL (Biological study)
(pharmaceutical tablet contg., effervescent)

IT **87-69-4**, biological studies
RL: BIOL (Biological study)
(pharmaceutical tablets contg., effervescent)

L34 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1990:65303 HCAPLUS
DN 112:65303
TI Use of different electropolymerization conditions for controlling the size-exclusion selectivity at polyaniline, polypyrrole and polyphenol films
AU Wang, Joseph; Chen, Shi Ping; Lin, Meng Shan
CS Dep. Chem., New Mexico State Univ., Las Cruces, NM, 88003, USA
SO J. Electroanal. Chem. Interfacial Electrochem. (1989), 273(1-2), 231-42
CODEN: JEIEBC; ISSN: 0022-0728
DT Journal
LA English
AB Controlled anodic growth of polyaniline, polyphenol, and polypyrrole films is exploited for changing their permeability to solute species. In particular, fine mol. wt. cutoffs are obtained by varying the electropolymn. time or monomer concn. The exclusion of large electroactive species offers substantial improvements in the selectivity of amperometric detection in flowing streams. For example, a judicious choice of the polymn. time allows selective flow injection measurements of catechol, H2O2, acetaminophen or hydrazine in the presence of excess of uric acid, **ascorbic** acid, chlorpromazine, or K ferrocyanide, resp. Complex chromatograms are greatly improved. Prevention of electrode deactivation due to protein adsorption is obsd. in the case of polyaniline films. Scanning electron micrographs show the microstructures of films following different anodization times. The electrochem. approach for making permselective coatings is very versatile because it provides an

elegant way of varying the transport properties.

IT **50-81-7, Ascorbic** acid, properties **58-68-4**, NADH **103-90-2**, Acetaminophen **120-80-9**, Catechol, properties **28930-19-0**, Methylcatechol
RL: PRP (Properties)
(permeation of, through conducting polymers, polymn. conditions effect on)

L34 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1987:512198 HCAPLUS
DN 107:112198
TI (Un)sulfonated polyarylsulfone or polyarylketone membranes for use in sensors and enzyme electrodes
IN Vadgama, Pankaj Maganlal; Mullen, William Henry; Scott, Graham Wilfred
PA Imperial Chemical Industries PLC, UK
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 225094	A2	19870610	EP 86-308918	19861114
	EP 225094	A3	19881214		
	EP 225094	B1	19911023		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 68824	E	19911115	AT 86-308918	19861114
	ES 2026458	T3	19920501	ES 86-308918	19861114
	ZA 8608715	A	19870729	ZA 86-8715	19861117
	AU 8665532	A1	19870604	AU 86-65532	19861120
	AU 595260	B2	19900329		
	US 4832797	A	19890523	US 86-936720	19861125
	IL 80753	A1	19900319	IL 86-80753	19861125
	NO 8604772	A	19870529	NO 86-4772	19861127
	NO 174897	B	19940418		
	NO 174897	C	19940727		
	FI 8604865	A	19870529	FI 86-4865	19861128
	FI 87932	B	19921130		
	FI 87932	C	19930310		
	DK 8605745	A	19870529	DK 86-5745	19861128
	JP 62132164	A2	19870615	JP 86-284073	19861128
	JP 07046085	B4	19950517		
	CA 1291956	A1	19911112	CA 86-524145	19861128
PRAI	GB 85-29300		19851128		
	EP 86-308918		19861114		

AB A membrane, permeable to liqs. and solutes, for use in a nonenzymic sensor or a sensor of the enzyme-electrode type, is formed from an (un)sulfonated polyarylsulfone (PAS) or an (un)sulfonated polyarylketone (PAK). A method for detg. an analyte comprises bringing the specimen into contact with the outer face of the membrane. For a membrane, 50 .mu.L of a 10% wt./vol. soln. of sulfonated polysulfone (sulfonation ratio 10) in DMSO was spread over a 20-cm2 glass plate and the plate was placed in a vacuum oven at 0.1 mm Hg and 50.degree. for 6 h. A soln. (10 .mu.L) contg. glucose oxidase 3

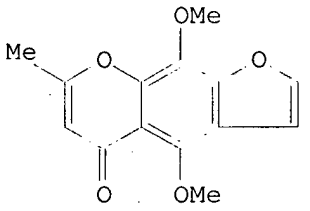
and serum albumin 200 mg/mL was mixed with a 5% **aq.** soln. of glutaraldehyde (5 .mu.L) and the mixt. was applied to 1 side of a polycarbonate film having pores of .apprx.0.015 .mu.m. A piece of the sulfonated polysulfone film was pressed onto the enzyme layer and the laminate was left to allow the enzyme to crosslink further. In the sensor, the laminate was positioned with the polysulfone layer facing the electrode. The polysulfone membrane layer screened out interfering species (e.g. **ascorbic** acid, **cysteine**, **glutathione**, urate, and acetaminophen) in a glucose assay.

IT **50-99-7**
RL: ANST (Analytical study)
(blood analysis, glucose detn. in, with enzyme electrode contg. sulfonated polysulfone layer in membrane for interfering species screening)

IT **50-99-7**, Glucose, analysis
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, with enzyme electrode contg. sulfonated polysulfone layer in membrane for interfering species screening)

IT **50-81-7**, uses and miscellaneous **103-90-2**, Acetaminophen
RL: USES (Uses)
(interference by, sulfonated polysulfone layer in glucose enzyme electrode membrane effect on)

L34 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1985:620724 HCAPLUS
DN 103:220724
TI A study of the effect of some drugs on the dissolution rate of khellin
AU Boraie, N. A.; Naggar, V. E.
CS Fac. Pharm., Alexandria Univ., Alexandria, Egypt
SO Farmaco, Ed. Prat. (1985), 40(10), 339-46
CODEN: FRPPAO; ISSN: 0430-0912
DT Journal
LA English
GI



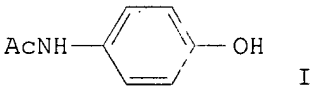
I

AB The dissoln. of Khellin (I) [82-02-0] was slightly higher in HCl than in **water** and followed 1st order kinetics at least in the 1st 30 min in the absence and in the presence of added drugs. Oxyphenonium bromide [50-10-2] in acid medium slightly enhanced I dissoln. rate. I soly. increased with increasing concn. of the former drug. I dissoln. rate also increased with increasing conc. of the other drugs. **Sulfathiourea** [515-49-1] decreased both the dissoln. rate and soly. of I in HCl at all concns. tested. Paracetamol [**103-90-2**], phenazone [60-80-0] and amidopyrine [58-15-1] appreciably decreased I dissoln. rate, although I soly. increased at all concns. of the analgesics tested. Caffeine

citrate [69-22-7], piperazine citrate [144-29-6] and to a lower extent promethazine-HCl [58-33-3] caused a substantial decrease in I dissoln. **Ascorbic** acid [**50-81-7**] gave an intermediate effect. Metformin-HCl [1115-70-4], nicotinamide [98-92-0], and cephalexin [15686-71-2] had only a small effect on dissoln. I dissoln. in either hexamine [100-97-0] or aminophylline [317-34-0] showed a different pattern in **water** from that in HCl.

IT **50-81-7**, uses and miscellaneous **103-90-2**
RL: BIOL (Biological study)
(dissoln. and soly. of Khellin in relation to)

L34 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 1999 ACS
AN 1981:24689 HCAPLUS
DN 94:24689
TI Evidence that acetaminophen and N-hydroxyacetaminophen form a common arylating intermediate, N-acetyl-p-benzoquinoneimine
AU Corcoran, G. B.; Mitchell, J. R.; Vaishnav, Y. N.; Horning, E. C.
CS Inst. Lipid Res., Baylor Coll. Med., Houston, TX, 77030, USA
SO Mol. Pharmacol. (1980), 18(3), 536-42
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
GI



I

AB Adding **ascorbic** acid [**50-81-7**] to microsomal incubations contg. acetaminophen (I) [**103-90-2**] inhibited covalent binding of the reactive metabolite. Adding **ascorbic** acid to incubations contg. acetaminophen and **cysteine** [52-90-4] markedly decreased acetaminophen-**cysteine** adduct [53446-10-9] formation. **Ascorbic** acid addn. to **aq.** incubations contg. N-hydroxyacetaminophen [63975-21-3] and **cysteine** similarly inhibited the nonenzymic formation of an acetoaminophen-**cysteine** adduct. Therefore, the chem. reactions responsible for the nonenzymic decompn. of N-hydroxyacetaminophen to yield acetaminophen-**cysteine** adducts were examd. In **aq.** solns. above pH 7, N-hydroxyacetaminophen rapidly dehydrated to N-acetyl-p-benzoquinoneimine [50700-49-7]. In the absence of reducing compds. N-acetyl-p-benzoquinoneimine reacted with another mol. of N-hydroxyacetaminophen to give equal amts. of nitrosophenol [104-91-6] and acetaminophen. The addn. of **cysteine** or **ascorbic** acid slowed the decompn. of N-hydroxyacetaminophen and inhibited the formation of nitrosophenol. **Cysteine** affected these changes through decreasing the concn. of N-acetyl-p-benzoquinoneimine, primarily by reducing it to acetaminophen at low pH (5.5-7.0) or by conjugating with it to yield an acetaminophen-**cysteine** adduct at high pH (7.5-11.0). **Ascorbic** acid produced its effects only through redn. of the N-acetyl-p-benzoquinoneimine intermediate; thus acetaminophen was the only product. Apparently, the reactive intermediate formed in microsomes from acetaminophen and in soln. from N-hydroxyacetaminophen is N-acetyl-p-benzoquinoneimine.

IT **50-81-7**, biological studies

RL: BIOL (Biological study)
(acetaminophen and hydroxyacetaminophen metabolic activation by liver microsomes response to)

IT **103-90-2**
RL: PROC (Process)
(metabolic activation of, by liver microsomes)

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=> D BIB ABS HITRN L28

L28 HAS NO ANSWERS
L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PARACETAMOL/CN
L2            14 SEA FILE=REGISTRY ABB=ON  PLU=ON  PARACETAMOL?/CN
L3            14 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2
L4          7451 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3
L5          1149 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND (AQUEOUS OR WATER OR
                 H2O)
L28            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND FREE
RADICAL(4A)SCAVENG
                 ?
```

=> d bib abs l21 1-3

L21 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:194666 SCISEARCH
GA The Genuine Article (R) Number: YZ716
TI Electrochemical poly(1,3-phenylenediamine) synthesis as enzyme immobilization media
AU Ekinci E; Ogunc S T; Karagozler A E (Reprint)
CS INONU UNIV, FAC ARTS & SCI, DEPT CHEM, TR-44069 MALATYA, TURKEY (Reprint);
INONU UNIV, FAC ARTS & SCI, DEPT CHEM, TR-44069 MALATYA, TURKEY
CYA TURKEY
SO JOURNAL OF APPLIED POLYMER SCIENCE, (4 APR 1998) Vol. 68, No. 1, pp. 145-152.
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0021-8995.
DT Article; Journal
FS PHYS; ENGI
LA English
REC Reference Count: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Electrochemical polymerization of the 1,3-phenylenediamine in the presence of **glucose** oxidase with KCl **aqueous** electrolyte at a potential of 0.800 V versus Ag-AgCl produces adherent poly(1,3-phenylenediamine) containing enzyme (**glucose** oxidase) film on a platinum electrode. Polymeric sensor prepared in this one-step procedure can be used to determine hydrogen peroxide formed as the result of the enzymatic reaction between **glucose** and **glucose** oxidase in the presence of O-2. The amperometric responses of the resultant enzyme electrode to **glucose** were rapid, reaching steady-state values within 4-5 s, and there was a linear relationship between **glucose** concentration and obtained current up to 6 mM. Polymeric sensor was stable for more 3 months. The **glucose** selectivity of enzyme electrode was determined in the presence of some interfering substances, such as lactose, **sucrose**, urea, uric acid, **paracetamol**, and **ascorbic** acid. Also, the effects of buffer concentration, storage conditions, and temperature on the steady-state amperometric responses were studied. Moreover, the Arrhenius activation energy for the enzymatic reaction was calculated.

L21 ANSWER 2 OF 3 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 88-072904 [11] WPIDS
DNN N88-055245 DNC C88-032700
TI Enzyme electrode membrane with base of alkoxy-substd. polyamide - having permeability to hydrogen peroxide or other polarographically detectable prods..
DC A96 B04 D16 J04 S03
IN SKELLY, P
PA (CAMB-N) CAMBRIDGE LIFE SCIENCES
CYC 1
PI GB 2194843 A 880316 (8811)* 7 pp
ADT GB 2194843 A GB 86-21555 860908
PRAI GB 86-21555 860908
AN 88-072904 [11] WPIDS

AB GB 2194843 A UPAB: 970424
An enzyme electrode membrane comprises an immobilised enzyme-contg. layer supported on a polymeric base layer permeable to H2O2 or other low mol.wt.
polarographically detectable species produced by reaction of the enzyme and a substance to be determined, where the polymeric base consists of or comprises a film of an alkoxy-substd. polyamide, pref. a methoxy-nylon (Elvamide; RTM (DuPont)). Pref. the surface of the enzyme-contg. layer is further protected by a microporous ultrafiltration membrane. An enzyme electrode biosensor incorporating the enzyme electrode member is also claimed.

The alkoxy-polyamide base layer is a spun coast film of thickness 0.5-1p, opt. also contg. a spun cast film of cellulose propionate (impermeable to **paracetamol**) and/or polyacrylic acid (impermeable to **ascorbate**). The enzyme is pref. **glucose** oxidase or cholesterol oxidase. The microporous ultrafiltration membrane comprises microporous polycarbonate, e.g. Nuclepore (RTM).

USE/ADVANTAGE - Useful for clinical or medical analysis of e.g. blood samples for uric acid, urea, drug molecules or esp. **glucose** or cholesterol (both claimed). The support is highly hydrophilic, with a high **water**-uptake, forming a hydrogel structure through which H2O2 etc. can readily diffuse. The support has good strength and good adhesion, both to the immobilised enzyme layer and to the outer protective layer, if used, giving robust membranes which are easy to clean, strong, and resistant to delamination and of good sensitivity. The base may include materials, e.g. sub-layers, which are resistant to the passage of interfering molecules such as **paracetamol** or **ascorbic** acid.
Dwg.0/2

L21 ANSWER 3 OF 3 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 84-177022 [28] WPIDS
DNC C84-074764
TI Effervescent tablets mfr. - using single appts. for mixing, humification and drying.
DC B07 P33
IN BRU, J
PA (REPR-N) RECH & PROPRIETE IND; (BRUJ-I) BRU J
CYC 17
PI WO 8402468 A 840705 (8428)* FR 20 pp
W: CH DE DK GB JP LU NL SE US
FR 2537872 A 840622 (8430)
PT 77864 A 841018 (8447)
DE 3390423 T 850124 (8505)
SE 8404142 A 840820 (8513)
GB 2146244 A 850417 (8516)
NL 8320404 A 850401 (8518)
JP 60500534 W 850418 (8522)
DK 8403979 A 840820 (8527)
FR 2555439 A 850531 (8527)
EP 162043 A 851127 (8548) FR
R: BE
ES 8603753 A 860516 (8627)
CA 1209040 A 860805 (8636)
US 4614648 A 860930 (8642)
GB 2146244 B 870128 (8704)

CH 664491 A 880315 (8816)
SE 457416 B 881227 (8903)
FR 2625434 A 890707 (8933)
EP 162043 B 891213 (8950) FR
R: BE
US 33086 E 891010 (8950)
IT 1175295 B 870701 (9029)
AT 8309080 A 911015 (9144)
KR 9007312 B 901008 (9201)
JP 07100653 B2 951101 (9548) 4 pp
DE 3390423 C2 960814 (9637) 8 pp

ADT WO 8402468 A WO 83-FR253 831220; FR 2537872 A FR 82-21476 821221; DE 3390423 T DE 83-3390423 831220; GB 2146244 A GB 84-27318 840229; NL 8320404 A NL 83-20404 831220; JP 60500534 W JP 84-500291 831220; FR 2555439 A FR 83-19143 831130; EP 162043 A EP 84-900064 831220; ES 8603753 A ES 83-528271 831221; US 4614648 A US 84-643980 840820; GB 2146244 B GB 83-27318 831220; FR 2625434 A FR 88-15535 881128; US 33086 E US 87-71991 870710; JP 07100653 B2 WO 83-FR253 831220, JP 84-500291 831220; DE 3390423
C2 DE 83-3390423 831220, WO 83-FR253 831220

FDT JP 07100653 B2 Based on JP 60500534, Based on WO 8402468; DE 3390423 C2 Based on WO 8402468

PRAI FR 83-19143 831130; FR 82-21476 821221

AN 84-177022 [28] WPIDS

AB WO 8402468 A UPAB: 951128
In the prepn. of effervescent tablets, wet mixing and drying/granulation are effected continuously in a single appts. Process comprises (a) premixing the reactants; (b) spraying with a liq. usually **water**, to 1-6% humidification the reactants being in an air-blown fluidised bed; and (c) drying, using the air from the fluidised bed, heated to 60-70 deg.C. This process may be carried out under a vacuum.

USE/ADVANTAGE - The process is of partic. use in the prepn. of aspirin and **paracetamol** tablets. It allows the components to be combined under conditions such that the effervescence is controlled, is simple and has a high throughput, The process gives a very uniform prod.. 2/2
Dwg.2/2

ABEQ EP 162043 B UPAB: 930925
Process for the preparation of effervescent tablets according to which the
powdered raw materials are treated in a granulation-drying device comprising heating means, and consisting in carrying out the granulation by addition of a granulating solvent in order to form granules by wetting,
and in drying the granules in vacuo, said granules being thereafter compressed into tablets, chracterised in that an apparatus is provided which is mounted vertically in order to form a dust-free working tower, in
which the raw materials are stored in hoppers situated near the upper part, and then gravity-fed in said granulation drying device; the raw materials are mixed in the granulation drying device, and then the granulating solvent is introduced in said device, the mixture of raw materials and granulating solvent is then stirred at the atmospheric pressure, until a granulation is obtained, and the granules are dried in vacuo, the dried raw materials are then cooled and finally the cooled dried raw materials are gravity-fed to a storage container.

ABEQ GB 2146244 B UPAB: 930925
A process of manufacture of effervescent granules, comprising adding powdered raw materials to a unitary mixer-granulator-drier, mixing the raw

materials therein, humidifying the mixture therein by spraying an **aqueous** solvent thereon to granulate the mixture at atmospheric pressure, and drying the mixture by creating a vacuum in the mixer-granulator-drier, the said unitary mixer-granulator-drier comprising
mixing means, means for spraying the solvent, means for regulating the temperature of the mixture, and means for creating the vacuum.

ABEQ US 33086 E UPAB: 930925

New process for mfr of effervescent tablets contg pharmaceutical comprises
steps of careful humidifying acid and base mixt, predrying and final drying and granulating operations are carried out in a single apparatus (high efficiency granulating tower), either integrally in fluid bed (Fig 1) or with vacuum drying, giving precise control of homogeneity of prod.

ADVANTAGE - Improved tablets.

ABEQ US 4614648 A UPAB: 930925

Process for mfg. effervessant tablets comprises mixing powdered raw materials, humidifying with solvent, granulation and drying in same appts.
applying vacuum for the drying step. For effervessant mixt. of NaHCO3 and
citric acid solvent is **water** with glycocoll opt. present.

Mixt. contg. **paracetamol** NaHCO3KHCO3 **sorbitol** anhydrous citric acid and **ascorbic** acid with soln. of manoxol in **water** as solvent. Another mixt. is Ca carbasalate, lysine carbonate and citric acid. Appts. comprises means for mixing (mechanical, stirrer/ lump breakers) and introduction of solvent (aspiration/vacuum/ spraying pump), temp. regulators (double jacket heat exchangers) and vacuum for drying with granules then cooling in heat exchanger. System is
fluid bed or vacuum drying.

ADVANTAGE - Simple economical process in single equipment gives improved uniform prod. Granulation is based on formation of mono- di- or
trisodium citrate by controlled humidification.

=> d l28 1-6 bib abs

L28 ANSWER 1 OF 6 MEDLINE DUPLICATE 2
AN 92226210 MEDLINE
DN 92226210
TI Determination of **paracetamol** and its four major metabolites in mouse plasma by reversed-phase ion-pair high-performance liquid chromatography.
AU Esteban A; Graells M; Satorre J; Perez-Mateo M
CS Division of Clinical Biochemistry, Hospital General de Elche, Alicante, Spain..
SO JOURNAL OF CHROMATOGRAPHY, (1992 Jan 3) 573 (1) 121-6.
Journal code: HQF. ISSN: 0021-9673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199207
AB A reversed-phase ion-pair high-performance liquid chromatographic method has been used for the separation of **paracetamol** and its four major metabolites (**glucuronide**, sulphate, **cysteine** and **mercapturate** conjugates) in mouse plasma samples. An ODS column was used and the mobile phase consisted of an **aqueous** solution of 0.01 M tetrabutylammonium chloride and 0.01 M Tris buffered to pH 5.0 with phosphoric acid, with methanol as the organic solvent. The gradient elution started with 30% methanol. After a delay of 0.5 min the methanol concentration was increased linearly to 75% over 7.5 min. The column was returned to the initial conditions after a delay of 1 min. A methanol solution of theophylline was added to the mouse plasma sample, centrifuged and immediately injected into the chromatographic system. The advantages of this method include good and rapid separation (last metabolite detected at 6.86 min), well resolved peaks, only a small amount of sample required for assay, adequate precision (no coefficient of variation was greater than 10% for **paracetamol** metabolites) and a high sensitivity (particularly for unchanged **paracetamol** and the **cysteine** conjugate).

L28 ANSWER 2 OF 6 MEDLINE DUPLICATE 3
AN 87195234 MEDLINE
DN 87195234
TI Automated liquid chromatographic method for the determination of **paracetamol** and six metabolites in human urine.
AU Ladds G; Wilson K; Burnett D
SO JOURNAL OF CHROMATOGRAPHY, (1987 Mar 6) 414 (2) 355-64.
Journal code: HQF. ISSN: 0021-9673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198708
AB An automated liquid chromatographic method, with a coefficient of variation for total imprecision of less than 4%, has been developed for the quantitative determination of **paracetamol**, **paracetamol**-4-**glucuronide**, **paracetamol**-4-sulphate, **paracetamol**-3-**cysteine**, **paracetamol**-3-**mercapturate**, 3-hydroxyparacetamol-3-

sulphate and 3-methoxyparacetamol-4-sulphate in urine samples. The gradient elution system was based on 0.067 M phosphate buffer (pH 2.0) and acetonitrile on an octadecylsilica column. The on-column detection limit using an ultraviolet detector at 254 nm for each of the compounds using 3-hydroxyacetanilide as internal standard was of the order of 10-50 ng from urine and 2-10 ng from **water**. Application of the method to 24-h urine samples from subjects who had received a therapeutic dose of the drug confirmed the findings of previous studies for the importance of the **glucuronide**, sulphate, mercapturate and cysteine conjugates. 3-Hydroxyparacetamol-3-sulphate was shown to be present in the urine of all volunteers and to account for up to 5% of the dose. 3-Methoxyparacetamol-4-sulphate was not detected in any urine samples and if present as a metabolite must account for less than 0.1% of the dose.

L28 ANSWER 3 OF 6 MEDLINE DUPLICATE 4
AN 78171764 MEDLINE
DN 78171764
TI Determination of **paracetamol** and its metabolites in urine by high-performance liquid chromatography using ion-pair systems.
AU Knox J H; Jurand J
SO JOURNAL OF CHROMATOGRAPHY, (1978 Feb 11) 149 297-312.
Journal code: HQF. ISSN: 0376-737X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197809
AB **Paracetamol** (P) and its four main metabolites, the sulphate (S), **glucuronide** (G), **cysteine** (C) and **mercapturic** acid (M) conjugates, are separated on ODS/TMS silica using a standard eluent, **water**-methanol-formic acid (86:14:0.1, v/v/v), in the order S, G, P, C, M. On addition of the ion-paring cations dioctylammonium (DOA) and tetrabutylammonium (TBA), the retention of S is vastly increased while those of G and M are substantially increased and that is C is reduced. The excessive retention of S and to a lesser extent that of M and G can be controlled by the addition of a suitable concentration of a co-ion such as nitrate. The order of elution is then G, C, P, M, S, although this can be varied by adjusting the amount of nitrate present. Loading of DOA is slow as it is very strongly adsorbed and typical concentrations in the eluent are below 7 mg/l. Loading by TBA is rapid with typical concentrations being around 200 mg/l. The effects of added co-ions such as nitrate can be explained in terms of simple ion-pair equilibria. Equilibration with respect to added salts is rapid. Application of the technique to analysis of therapeutic and overdose urines shows the presence of at least three additional metabolites, one of which is identified by mass spectrometry as most probably 3-methoxyparacetamol. Another appears to be a methoxymercapturic acid derivative. There is further evidence for a group of metabolites that elute unresolved from overdose urines as a broad band after the main metabolites.

L28 ANSWER 4 OF 6 MEDLINE
AN 78026729 MEDLINE
DN 78026729

TI Determination of **paracetamol** and its metabolites in urine by high-performance liquid chromatography using reversed-phase bonded supports.
AU Knox J H; Jurand J
SO JOURNAL OF CHROMATOGRAPHY, (1977 Nov 11) 142 651-70.
Journal code: HQF. ISSN: 0021-9673.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197802
AB **Paracetamol** and its four main metabolites, the sulphate (S), **glucuronide** (G), **cysteine** (C) and **mercapturic** acid (M) conjugates, are readily separated in a synthetic mixture using slightly acidic **aqueous** alcoholic eluents (e.g. **water** -methanol-formic acid, 85:15:0.15, v/v/v) on either octadecyl silica (ODS silica) or octadecyl silica which has been further silanized to remove residual hydroxyl groups (ODS/TMS silica). The dependences of k' upon alcohol, acid and added salt concentrations are reported for both materials. The latter material gives the higher plate efficiencies and is much superior when applied to analysis of urines taken after therapeutic doses and overdoses of **paracetamol**. At least four additional metabolites are reported in overdose urines. Mass spectrometric analysis (high and low resolution) has confirmed the identity of M and identified one of the additional metabolites as methoxyparacetamol. Mass spectra of the remaining additional metabolites enable major structural features to be deduced. One of these metabolites may be associated with liver damage.

L28 ANSWER 5 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.DUPLICATE 1
AN 1999013761 EMBASE
TI Direct determination of **paracetamol** and its metabolites in urine and serum by capillary electrophoresis with ultraviolet and mass spectrometric detection.
AU Heitmeier S.; Blaschke G.
CS G. Blaschke, Institute Pharmaceutical Chemistry, University of Munster, Hittorfstrasse 58-62, 48149 Munster, Germany
SO Journal of Chromatography B: Biomedical Applications, (1999) 721/1 (93-108).
Refs: 30
ISSN: 0378-4347 CODEN: JCBBEP
PUI S 0378-4347(98)00415-0
CY Netherlands
DT Journal; Article
FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The use of capillary electrophoresis (CE) for the determination of **paracetamol** and its main metabolites in urine and serum is described. Due to its high efficacy, CE enables the analysis of drugs directly in complex matrices. Thus, simple, rapid and reliable assays could be developed that made use of some of the main advantages of this analytical technique. In order to prevent the peaks from tailing, a **water** zone was injected behind the sample. Occasionally occurring peak splittings of **paracetamol** were investigated and methods to suppress these splittings were developed. **Paracetamol**, its main metabolites, **paracetamol glucuronide**, **paracetamol** sulfate as well as **paracetamol**

cysteinate and **paracetamol mercapturate**, as metabolites of the oxidative pathway were identified in urine using diode-array detection and coupling of the CE instruments to electrospray-mass spectrometry. The assays were validated. Their usefulness was demonstrated by applying them to the analysis of urine and serum samples of healthy volunteers as well as to urine samples from children under anticancer therapy.

L28 ANSWER 6 OF 6 EMBASE
AN 87025256 EMBASE
DN 1987025256
TI High-performance liquid chromatography systems for the analysis of analgesic and non-steroidal anti-inflammatory drugs in forensic toxicology.
AU Stevens H.M.; Gill R.
CS Central Research Establishment, Home Office Forensic Science Service, Reading, Berkshire, RG7 4PN, United Kingdom
SO Journal of Chromatography, (1986) 370/1 (39-47).
CODEN: JOCRAM
CY Netherlands
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
052 Toxicology
049 Forensic Science Abstracts
LA English
AB High-performance liquid chromatography retension data are presented for over 40 analgesic drugs on an ODS-silica packing material to assist in the identification of these compounds. Three isocratic eluents prepared from isopropanol, formic acid and an **aqueous** phosphate buffer have been used. One eluent has been used for the analysis of **paracetamol** in whole blood.

=> d his

(FILE 'HOME' ENTERED AT 07:05:59 ON 01 MAR 1999)

FILE 'REGISTRY' ENTERED AT 07:07:44 ON 01 MAR 1999
L1 1 S PARACETAMOL/CN

FILE 'MEDLINE, BIOSIS, EMBASE, CEN, DRUGB, DRUGNL, JICST-EPLUS, LIFESCI, SCISEARCH, WPIDS' ENTERED AT 07:09:03 ON 01 MAR 1999

FILE 'REGISTRY' ENTERED AT 07:09:13 ON 01 MAR 1999
SET SMARTSELECT ON
L2 SEL L1 1- CHEM : 83 TERMS
SET SMARTSELECT OFF

FILE 'MEDLINE, BIOSIS, EMBASE, CEN, DRUGB, DRUGNL, JICST-EPLUS, LIFESCI, SCISEARCH, WPIDS' ENTERED AT 07:09:15 ON 01 MAR 1999
L3 49089 S L2
L4 49089 S PARACETAMOL OR L3
L5 2027 S L4 AND (AQUEOUS OR WATER OR H2O)
L6 160 S L5 AND (POLYHYDRIC OR INOSITOL OR SORBIT? OR GLYCEROL OR SUG
L7 308 S L5 AND (SUCROSE OR FRUCTOSE OR ASCORB? OR GLUC?)
L8 0 S L5 AND (PROPANE DIOL OR DIHYDROXYPROPANE)
L9 432 S L6 OR L7
L10 0 S L9 AND (BUBBL?)
L11 30 S L9 AND BUFFER?
L12 60 S PARACETAMOL(20A)BUFFER?
L13 3 S L12 AND L9
L14 0 S L9 AND FREE RADICAL(9A)SCAVANG?
L15 242 S L5 AND (SUCROSE OR FRUCTOSE OR GLUC?)
L16 368 S L6 OR L8 OR L15
L17 0 S L16 AND ASCORB? AND FREE RADICAL
L18 35 S L16 AND ASCORB?
L19 3 S L16 AND ASCORB?(9A)PARACETAMOL
L20 3 DUP REMOV L19 (0 DUPLICATES REMOVED)
L21 3 S L16 AND ASCORB?(19A)PARACETAMOL
L22 50 S L16 AND (THIO? OR MERCAPT? OR CYSTEIN? OR ETHANESULFON? OR T
L23 10 S L16 AND (ACETYLCYST? OR MERCAPTOETHANE?)
L24 57 S L22 OR L23
L25 0 S L16 AND (ACETYLCYST? OR MERCAPTOETHANE?)(20A)PARACETAMOL
L26 0 S L16 AND (ACETYLCYST? OR MERCAPTOETHANE?)(30A)PARACETAMOL
L27 13 S L16 AND (THIO? OR MERCAPT? OR CYSTEIN? OR ETHANESULFON? OR T
L28 6 DUP REMOV L27 (7 DUPLICATES REMOVED)
L29 0 S L16 AND (DITHIOTHREIT? OR REDUCED?(3A)GLUTATHION OR ETHANESU
L30 0 S L16 AND ISOTONIZ?
L31 2 S L16 AND STERLI?
L32 0 S L16 AND (CNS OR CENTRAL NERVOUS)(9A)ANALGES?
L33 11 S L16 AND (MORPHIN?)
L34 27 S L16 AND (COMPLEX? OR CHELAT?)
L35 3 S L34 AND STABL?
L36 1 S L16 AND (COMPLEX? OR CHELAT?)(20A)PARACETAMOL
L37 4 S L35 OR L36
L38 7 DUP REMOV L33 (4 DUPLICATES REMOVED)
L39 0 S L16 AND (PHENYLPIPERIDIN? OR NIPECOTIC OR PHENYLCYCLOHEXANOL
L40 0 S L16 AND PHENYLAZEPINE
L41 14 S L16 AND (ANTIINFLAM? OR ANTI INFLAM? OR NSAI? OR KETOPROF?)
L42 14 S L16 AND (IBUPROFEN OR FENOPROFEN OR FLURIBIPROFEN?)
L43 24 S L41 OR L42

L44	2	S L43 AND STABL?
L45	4	S L43 AND KETOPROF?
L46	0	S L16 AND (ANTIMETIC OR DIMENHYDRIN OR DIPHENIDOL)
L47	2	S L16 AND (GRANISETRON OR MECLIZINE OR ONDANSETRON)
L48	3	S L16 AND (PROCHLORPERAZ? OR PROMETHAZIN? OR SCOPOLAMINE?)
L49	0	S L16 AND (THIETHYLPERAZINE OR TRIMETHOBENZAMID?)
L50	4	S L46-L49
L51	4	DUP REMOV L50 (0 DUPLICATES REMOVED)
L52	5	S L16 AND (ANTIEPILEP? OR CARBAMAZ? OR DIVALPRO? OR FELBAMATE?
L53	13	S L16 AND (GABAPENTIN OR PHENOBARBITAL OR PHENYLTROIN)
L54	1	S L16 AND (PHENSUXIMIDE OR VALPROIC)
L55	19	S L52-L54
L56	19	S L52 OR L53 OR L54
L57	0	S L52 AND STABL?
L58	0	S L53 AND STABL?
L59	0	S L54 AND STABL?
L60	12	S L16 AND (CORTICOSTEROID? OR HYDROCORTIS?)
L61	0	S L16 AND TRICYCLIC ANTIDEPRESS?
L62	5	S L16 AND (AMITRIPTYL? OR CLOMIPRAMIN? OR DOXEPIN)
L63	1	S L16 AND (IMIPRAMINE OR TRIMIPRAMINE)
L64	1	S L16 AND (AMOXAPINE OR DESIPRAMINE OR NORTRIPTYLINE OR PROTRI
L65	6	S L62 OR L63 OR L64

=> d bib abs l37 1-4

L37 ANSWER 1 OF 4 CEN COPYRIGHT 1999 ACS

AN 91:2783 CEN
TI Air Pollution and Forest Damage
Regional air pollution is one of the man-made stresses causing gradual and subtle changes over wide, forested areas of the U.S. and Canada
AU Smith, William H.
CS Yale University
SO Chemical & Engineering News, (11 Nov 1991) Vol. 69, No. 45, pp. 30. CODEN: CENEAR, ISSN: 0009-2347.
PB American Chemical Society
LA English
WC 8568

L37 ANSWER 2 OF 4 JICST-EPlus COPYRIGHT 1999 JST
AN 960046608 JICST-EPlus
TI Amperometric Biosensors Using Poly-L-Lysine/Poly-(styrenesulfonate) Membranes with Immobilized Enzymes.
AU MIZUTANI F; YABUKI S; HIRATA Y
CS National Inst. Biosci. and Human-Technol., Ibaraki, JPN
SO Denki Kagaku oyobi Kogyo Butsuri Kagaku, (1995) vol. 63, no. 12, pp. 1100-1105. Journal Code: G0072A (Fig. 7, Tbl. 1, Ref. 23) ISSN: 0366-9297
CY Japan
DT Journal; Article
LA English
STA New
AB Enzyme electrodes for L-lactic acid, choline and **glucose** were prepared by immobilizing lactate oxidase, choline oxidase and **glucose** oxidase into polyion **complex** membranes, respectively: an **aqueous** solution containing poly-L-lysine and each enzyme was placed on a glassy carbon electrode, then an **aqueous** solution of poly(4-styrenesulfonate) was added to the polycation/enzyme mixture and dried. The anodic current (at 1 V vs. Ag/AgCl) of each enzyme electrode increased after the addition of the corresponding analyte, due to the electrolytic oxidation of the hydrogen peroxide produced through the oxidase-catalyzed reaction in the membrane. The membrane showed permselectivity based on the solute size with the molecular cut-off of 110. For the L-lactate and choline-sensing electrodes, the permselectivity was effective in reducing the interferential response as compared to the response for the analyte: the permeation of interferents such as L-ascorbic acid, uric acid and **acetaminophen**, was restricted, whereas the analyte permeated easily to undergo the enzymatic reaction. In the case of the **glucose** oxidase/polyion **complex** layer, the restriction of **glucose** transport resulted in the enzyme electrode suitable for the determination of the analyte in high concentrations. Each enzyme electrode was highly **stable**, e.g., the **glucose**-sensing electrode could be used for more than 20 weeks. (author abst.)

L37 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 96:24006 SCISEARCH
GA The Genuine Article (R) Number: TK612
TI AMPEROMETRIC BIOSENSORS USING POLY-L-LYSINE/POLY(STYRENESULFONATE) MEMBRANES WITH IMMOBILIZED ENZYMES
AU MIZUTANI F (Reprint); YABUKI S; HIRATA Y

CS NATL INST BIOSCI & HUMAN TECHNOL, 1-1 HIGASHI, TSUKUBA, IBARAKI 305, JAPAN
(Reprint)
CYA JAPAN
SO DENKI KAGAKU, (DEC 1995) Vol. 63, No. 12, pp. 1100-1105.
ISSN: 0366-9297.
DT Article; Journal
FS PHYS; ENGI
LA ENGLISH
REC Reference Count: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Enzyme electrodes for L-lactic acid, choline and **glucose** were prepared by immobilizing lactate oxidise, choline oxidase and **glucose** oxidase into polyion **complex** membranes, respectively: an **aqueous** solution containing poly-L-lysine and each enzyme was placed on a glassy carbon electrode, then an **aqueous** solution of poly(4-styrenesulfonate) was added to the polycation/enzyme mixture and dried. The anodic current (at 1 V vs. Ag/AgCl) of each enzyme electrode increased after the addition of the corresponding analyte, due to the electrolytic oxidation of the hydrogen peroxide produced through the oxidase-catalyzed reaction in the membrane. The membrane showed permselectivity based on the solute size with the molecular cut-off of 110. For the L-lactate and choline-sensing electrodes, the permselectivity was effective in reducing the interferential response as compared to the response for the analyte: the permeation of interferents such as L-ascorbic acid, uric acid and **acetaminophen**, was restricted, whereas the analyte permeated easily to undergo the enzymatic reaction. in the case of the **glucose** oxidase/polyion **complex** layer, the restriction of **glucose** transport resulted in the enzyme electrode suitable for the determination of the analyte in high concentrations. Each enzyme electrode was highly **stable**, e.g., the **glucose**-sensing electrode could be used for more than 20 weeks.

L37 ANSWER 4 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 84-144236 [23] WPIDS
DNC C84-061203
TI Stabilising and masking unpleasant taste of **aq**. **paracetamol** suspension - by combining with sodium CMC **sorbitol**, citric acid, colloidal aluminium and silicon **complex**, sweetener, aromatiser etc..
DC A96 B05
IN BALOESCU, C; CONDURACHE, M; GITLAN, F; TRIFANESCU, D
PA (CONT-N) INST CONTROL STAT MED; (BIOB) INTR MEDICAMENTE BIOFARM
CYC 1
PI RO 82841 A 831030 (8423)*
ADT RO 82841 A RO 81-105031 810804
PRAI RO 81-105031 810804
AN 84-144236 [23] WPIDS
AB RO 82841 A UPAB: 930925
The suspension contains 1-2.5% **paracetamol** combined with 0.3-1.5% NaCMC, 30-50% **sorbitol**, 0.1-0.3% citric acid, 0.3-0.6% colloidal complex of Al and Si with the addn. of sweetener, stabiliser, colouring material and aromatiser, using **water** as vehicle.
The suspension has good physical and chemical stability, a pleasant smell and the unpleasant taste is masked.

=> d bib abs l31 1-2

L31 ANSWER 1 OF 2 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 87109186 EMBASE
DN 1987109186
TI Automated liquid chromatographic method for the determination of **paracetamol** and six metabolites in human urine.
AU Ladds G.; Wilson K.; Burnett D.
CS Department of Biological and Environmental Sciences, The Hatfield Polytechnic, Hatfield, Hertfordshire AL10 9AB, United Kingdom
SO Journal of Chromatography - Biomedical Applications, (1987) 414/2 (355-364).
CODEN: JCBADL
CY Netherlands
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
LA English
AB An automated liquid chromatographic method, with a coefficient of variation for total imprecision of less than 4%, has been developed for the quantitative determination of **paracetamol**, **paracetamol**-4-**glucuronide**, **paracetamol**-4-sulphate, **paracetamol**-3-cysteine, **paracetamol**-3-mercapturate, 3-hydroxyparacetamol-3-sulphate and 3-methoxyparacetamol-4-sulphate in urine samples. The gradient elution system was based on 0.067 M phosphate buffer (pH 2.0) and acetonitrile on an octadecylsilica column. The on-column detection limit using an ultraviolet detector at 254 nm for each of the compounds using 3-hydroxyacetanilide as internal standard was of the order of 10-50 ng from urine and 2-10 ng from **water**. Application of the method to 24-h urine samples from subjects who had received a therapeutic dose of the drug confirmed the findings of previous studies for the importance of the **glucuronide**, sulphate, mercapturate and cysteine conjugates. 3-Hydroxyparacetamol-3-sulphate was shown to be present in the urine of all volunteers and to account for up to 5% of the dose. 3-Methoxyparacetamol-4-sulphate was not detected in any urine samples and if present as a metabolite must account for less than 0.1% of the dose.

L31 ANSWER 2 OF 2 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 87025256 EMBASE
DN 1987025256
TI High-performance liquid chromatography systems for the analysis of analgesic and non-steroidal anti-inflammatory drugs in forensic toxicology.
AU Stevens H.M.; Gill R.
CS Central Research Establishment, Home Office Forensic Science Service, Reading, Berkshire, RG7 4PN, United Kingdom
SO Journal of Chromatography, (1986) 370/1 (39-47).
CODEN: JOCRAM
CY Netherlands
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
052 Toxicology
049 Forensic Science Abstracts
LA English

AB High-performance liquid chromatography retension data are presented for over 40 analgesic drugs on an ODS-silica packing material to assist in the identification of these compounds. Three isocratic eluents prepared from isopropanol, formic acid and an **aqueous** phosphate buffer have been used. One eluent has been used for the analysis of **paracetamol** in whole blood.

=> d bib abs l38 1-7

L38 ANSWER 1 OF 7 MEDLINE DUPLICATE 1
AN 91292946 MEDLINE
DN 91292946
TI Drug metabolizing enzyme changes after chronic buthionine sulfoximine exposure modify **acetaminophen** disposition in rats.
AU Manning B W; Franklin M R; Galinsky R E
CS Department of Pharmacology, College of Pharmacy, University of Utah, Salt Lake City 84112.
NC GM 39335 (NIGMS)
AG 07135 (NIA)
SO DRUG METABOLISM AND DISPOSITION, (1991 Mar-Apr) 19 (2) 498-502.
Journal code: EBR. ISSN: 0090-9556.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199110
AB This study examined the effects of prolonged exposure to buthionine sulfoximine (BSO) on 1) the overall elimination pharmacokinetics of **acetaminophen**; 2) the sulfate and **glucuronide** conjugation processes primarily responsible for **acetaminophen** elimination; and 3) in vitro microsomal and cytoplasmic enzyme activities in rats. Rats imbibed drinking **water** containing 30 mM BSO for 6 days and then received an iv injection of **acetaminophen**, 150 mg/kg in a propylene **glycol** vehicle. Exposure to BSO, a specific inhibitor of gamma-glutamylcysteine synthetase, produced marked depletion of glutathione (GSH) and resulted in induction of hepatic UDP-**glucuronosyltransferase** and GSH-S-transferase enzyme activities, but not cytochrome P-450. BSO pretreatment had no effect on the total or renal clearance of **acetaminophen** in rats. However, BSO exposure increased the partial clearance of **acetaminophen** to **acetaminophen glucuronide** by 47% (1.29 +/- 0.08 vs. 1.90 +/- 0.23 ml/min/kg; p less than 0.01) and significantly (p less than 0.02) increased the percentage of the dose recovered as the **glucuronide** conjugate from 17.6 +/- 2.5 to 26.5 +/- 0.6 The partial clearance of **acetaminophen** to **acetaminophen** sulfate was decreased, although not significantly, from 4.46 +/- 0.62 to 3.39 +/- 0.82 ml/min/kg.
BSO treatment increased microsomal UDP-**glucuronosyltransferase** activity toward three xenobiotic aglycones, p-nitrophenol, 1-naphthol, and **morphine** by 308, 61, and 66%, respectively (p less than 0.05), but not toward testosterone or estrone. Cytosolic GSH-S-transferase activity toward 1-chloro-2,4-dinitrobenzene was increased 52% by BSO, whereas p-nitrophenol sulfotransferase activity was not altered. Cytochrome P-450 concentration and monooxygenase activity were unchanged by BSO exposure.

L38 ANSWER 2 OF 7 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V. DUPLICATE 2
AN 91106833 EMBASE
DN 1991106833
TI Acute pain in children and its treatment.
AU Dalens B.
CS Departement d'Anesthesie-Reanimation, Pavillon Gosselin, Hotel-Dieu, BP 69, 63003 Clermont-Ferrand Cedex, France
SO Annales Francaises d'Anesthesie et de Reanimation, (1991) 10/1 (38-61).

ISSN: 0750-7658 CODEN: AFAREO
CY France
DT Journal; General Review
FS 007 Pediatrics and Pediatric Surgery
024 Anesthesiology
037 Drug Literature Index
LA French
SL English

AB Pain in paediatrics has long been underestimated. The numerous scientific studies carried out during the last decade show that its existence can no longer be doubted: in fact, pain already exists during the neonatal period, and probably throughout the last trimester of gestation as well. Pain pathways mature during the embryonic period and peripheral receptors develop between the 7(th) and 20(th) week. A-delta and C fibers, as well as spinal roots and nerves, are completely differentiated before the end of the second month. The development of specific neurotransmitters and thalamic and cortical dendritic branching occurs later on; it is well enough developed to allow perception of painful stimuli (slow or protopathic component) from the beginning of the foetal period onwards. The discriminative rapid component develops in parallel to myelinisation, and the psycho-affective component, which requires a long and complex learning process, will not be fully operative until the end of puberty. Assessing pain, already a difficult task in the adult, is all the more so in children because of lesser verbal communicative capabilities, difficulty in handling abstract concepts, lack of experience of painful stimuli to make comparisons, and ignorance of their body image. In the very young child, diagnosing pain relies on suggestive circumstances, and an altered behaviour, knowing that no one symptom is pathognomonic. As the child grows up, methods for self-assessment of pain become usable, such as coloured scales and simplified verbal scales. However, behavioural tests remain the mainstay until the prepubertal period. The treatment of acute pain requires a reasoned approach which takes into account the state of the child, that of the aetiological investigations, the likely course of the lesions, as well as the patient's analgesic requirements. Therapeutic means do not differ from those for adult patients; however, the differences of distribution of body **water**, the small possibilities of linking with plasma proteins, and limited conjugation with **glucuronate** must be taken into account, especially during the first months of life. Local and regional anaesthetic block techniques are of great interest in elective and emergency surgery, as well as in trauma: they can provide complete pain relief, mostly without having any effect on the patient's physiological state (haemodynamics and consciousness). Peripherally acting analgesic agents, which are well supported on the whole, as well as co-analgesics, have a great part to play, although there are less drugs available than for adults. The most useful ones are **paracetamol**, followed by the salicylates, propionic acid derivatives and non steroid anti-inflammatory drugs. The restricted efficacy of these drugs often means that centrally acting analgesics, mostly **morphine**, need to be used. As well as the usual means of giving analgesic drugs, there are now new promising techniques of analgesic administration. Whilst transdermal patches of central analgesics are still experimental, analgesia controlled by the (old) child are beginning to be used routinely; however, these require special equipment (servo-controlled syringe pump), personnel and installations which are not available everywhere. It is now forbidden to neglect pain in children, because of the seriousness with which scientific

studies have been carried out in paediatrics for the last few years; increasingly reliable assessment scales, precise pharmacological studies and large scale evaluation of different local, regional and general analgesic methods mean that children must get pain relief, which is a right for all human beings.

L38 ANSWER 3 OF 7 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 82174099 EMBASE
DN 1982174099
TI [Intoxication by **water** and antidiuresis conditions].
LES INTOXICATIONS PAR L'EAU ET LES ETATS D'ANTIDIURESE.
AU Rince M.; Charmes J.P.; Leroux-Robert C.
CS Serv. Nephrol., CHU Dupuytren, 87000 Limoges, France
SO Revue du Praticien, (1982) 32/21 (1427-1439).
CODEN: REPRA3
CY France
DT Journal
FS 038 Adverse Reactions Titles
037 Drug Literature Index
003 Endocrinology
028 Urology and Nephrology
LA French
SL English

L38 ANSWER 4 OF 7 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 81110922 EMBASE
DN 1981110922
TI Specific modalities of therapy for inappropriate antidiuretic hormone secretion.
AU Sordillo P.; Matarese R.A.; Novich R.K.; et al.
CS Nephrol. Sect., Dept. Med., Lenox Hill Hosp., New York, N.Y. 10021, United States
SO Clinical Nephrology, (1981) 15/3 (107-110).
CODEN: CLNHBI
CY Germany
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
LA English
AB In addition to general therapeutic maneuvers which will correct hypoosmolality in all patients with SIADH, there also exist precise remedies which can successfully treat SIADH in a specific manner. When the diagnosis of SIADH is made, general measures such as **water** restriction and salt replacement should be started, and more vigorous therapeutic maneuvers such as the use of concentrated salt solutions and diuretics should be considered. In addition, however, consideration must also be given to the specific type of SIADH that is to be treated. As illustrated, if endogenous excessive ADH secretion has resulted either from a drug which stimulates ADH release, or from stimuli arising elsewhere in the organism such as may occur with extensive pulmonary or central nervous system disease, use of an agent which can suppress ADH secretion, such as phenytoin, in usual doses, should be considered. Furthermore, if SIADH secondary to neoplasm is encountered, the use of demeclocycline, an agent which blocks ADH effect at the level of the collecting tubule, will prove most efficacious. This agent may be used in low doses for extended periods of time if necessary, if careful follow-up for evidence of renal, or other, toxicity is made. Finally, the diagnosis

of **glucocorticoid** deficiency should always be considered when SIADH is encountered since this disorder can be rapidly corrected by **glucocorticoid** administration. In addition, this diagnosis may also alert the physician to the possibility of other serious hormone deficiencies.

L38 ANSWER 5 OF 7 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 74185907 EMBASE
DN 1974185907
TI The use of diamorphine in the management of terminal cancer.
AU Twycross R.G.
CS St Christopher's Hosp., London, United Kingdom
SO J.THANATOLOGY, (1972) 2/3-4 (733-743).
CODEN: JTHNA2
DT Journal
FS 037 Drug Literature Index
020 Gerontology and Geriatrics
006 Internal Medicine
016 Cancer
009 Surgery
LA English
AB Although the majority of patients with pain problems at St. Christopher's and St. Joseph's receive diamorphine there is a minority who are maintained on a variety of other analgesics ranging from aspirin and **paracetamol** to dextropropoxyphene and the synthetic narcotics such as pentazocine and phenazocine. Of the majority who receive diamorphine, only 15% have it by injection throughout their time in hospital. The remainder take it as an oral mixture consisting of diamorphine 2.5 mg or more, cocaine 10 mg, ethyl alcohol (95%) 2.5 ml, syrup (66% **sucrose** in **water**) 5 ml, made up to 20 ml by the addition of chloroform **water**. These patients are maintained on a suitable dose given regularly every 4 hr to prevent the recurrence of pain. The right dose is that dose which keeps the patient free of pain. With the aid of a night sedative most patients do not require a 2:00 a.m. dose. A tradition has developed whereby almost all patients receive a phenothiazine syrup with the diamorphine mixture, usually either prochlorperazine or chlorpromazine. Originally given to relieve coexistent nausea or vomiting, it is now also given to mask the bitter taste of diamorphine. Unfortunately, just over 1% of the patients admitted with severe pain fail to obtain adequate relief, and a further 20%, although much relieved, do experience pain from time to time especially when moved.

L38 ANSWER 6 OF 7 LIFESCI COPYRIGHT 1999 CSA
AN 97:6702 LIFESCI
TI Sulphation catalysed by the human cytosolic sulphotransferases-chemical defence or molecular terrorism?
AU Coughtrie, M.W.H.
CS Dep. Biochem. Med., Univ. Dundee, Ninewells Hosp. and Med. Sch., Dundee DD1 9SY, UK
SO HUM. EXP. TOXICOL., (1996) vol. 15, no. 7, pp. 547-555.
ISSN: 0144-5952.
DT Journal
FS X
LA English
AB The abundance of toxic and biologically active chemicals in our internal and external environments represents a serious threat to health. To combat

this threat, we have evolved a complex and effective chemical defence system comprising, among other components, a series of enzyme families whose main function is generally accepted to be the detoxification of xenobiotics and endogenous toxins. These so-called drug (or xenobiotic) metabolising enzymes classically act upon toxic or potentially toxic chemicals to reduce their biological activity and increase their **water** solubility, thereby facilitating removal from the body and achieving detoxification. In this somewhat oversimplified view, drug metabolising enzymes can be seen to contribute to either Phase I (i.e. functionalisation) or Phase II (i.e. conjugation) of drug metabolism. For example, a xenobiotic such as benzene is converted to phenol by the action of cytochrome P450 (aromatic hydroxylation - Phase I), which in turn can be conjugated with **glucuronic** acid (catalysed by UDP-**glucuronosyltransferase** Phase II) to form phenyl **glucuronide** which is readily excreted in the urine due to its increased polarity and **water** solubility. This classical view, however, masks many practical aspects of the way our bodies respond to chemical challenge. For instance, numerous compounds can be directly conjugated without the need for a functionalisation reaction as they already contain the appropriate functional group (**paracetamol** is one of the more common examples) and, more sinisterly, many compounds to which we are exposed are rendered more biologically active following metabolism - i.e. they are bioactivated. This can be exploited pharmacologically, through prodrugs which require metabolism to form the active compound (e.g. the O-demethylation of codeine by cytochrome P450 to form **morphine**; the sulphation of minoxidil by sulphotransferase to form minoxidil sulphate). However, this same phenomenon of bioactivation is central to the mechanism of action of numerous chemical carcinogens and other toxins. Understanding the underlying mechanisms and consequences of this duplicitous behaviour of xenobiotic metabolising enzymes is essential if we are to fully appreciate their biological function and such knowledge may direct us towards new approaches to the treatment and/or prevention of chemical-induced toxicity. In addition to its place in the body's chemical defence armoury, the central role of sulphation in the bioactivation of numerous chemical carcinogens such as aromatic amines and benzylic alcohols of polycyclic aromatic hydrocarbons has long been recognised (reviewed in). The recent surge of interest in sulphation and advances in the molecular analysis of sulphotransferases, suggests an appraisal of the biological and toxicological significance of sulphation is timely. The purpose of this article is to explore the functions of sulphation in detoxification and bioactivation and to examine some of the genetic and environmental factors which may determine the relative importance of these conflicting facets of sulphation reactions.

L38 ANSWER 7 OF 7 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 98-437043 [37] WPIDS
DNC C98-132804
TI New burst-free, sustained, programmable release composition(s) - containing an active material in a blend of uncapped and end-capped co polymer, preferably a poly (DL-lactide-co glycolide).
DC A96 B04 B05 B07 D16
IN BOEDEKER, E C; FRIDEN, P; JACOB, E; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; TICE, T R; VAN HAMONT, J E
PA (USSA) US SEC OF ARMY
CYC 79
PI WO 9832427 A1 980730 (9837)* EN 422 pp

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9863175 A 980818 (9851)

ADT WO 9832427 A1 WO 98-US1556 980127; AU 9863175 A AU 98-63175 980127

FDT AU 9863175 A Based on WO 9832427

PRAI US 97-789734 970127

AN 98-437043 [37] WPIDS

AB WO 9832427 A UPAB: 980916

A composition is claimed for the burst-free, sustained, programmable release of active material(s) over a period from 1-100 days, comprising: (a) an active material; and (b) a carrier which may contain pharmaceutically-acceptable adjuvant, comprised of a blend of uncapped and end-capped biodegradable-biocompatible copolymer.

Also claimed are: (1) a process for preparing controlled release compositions characterised by burst-free, sustained, programmable release of biologically active agents, comprising: (a) dissolving biodegradable poly(lactide/glycolide), in uncapped or end-capped form in methylene chloride, and dissolving a biologically active agent or active core in **water**; (b) adding the **aqueous** layer to the polymer solution and emulsifying to provide an inner **water**-in-oil (w/o) emulsion; (c) stabilising the w/o emulsion in a solvent-saturated **aqueous** phase containing a oil-in-**water** (o/w) emulsifier; (d) adding the w/o emulsion to an external **aqueous** layer containing o/w emulsifier to form a ternary emulsion; and (e) stirring the resulting **water**-in-oil-in-**water** (w/o/w) emulsion to remove the solvent, and rinsing hardened microcapsules with **water** and lyophilising the hardened microcapsules; (2) a method for the protection against infection of a mammal by pathogenic organisms comprising administering orally to the mammal an immunogenic amount of an immunostimulating composition consisting of an antigenic synthetic peptide encapsulated within a poly(lactide/galactide) matrix; (3) a vaccine for the immunisation of a mammal against infection by pathogenic organisms consisting of an antigen in an amount of 0.1-1% encapsulated within a biodegradable-biocompatible polymeric poly(DL-lactide-co-glycolide) matrix where the polymer is end-capped or a blend of uncapped and end-capped polymers; and (4) an immunostimulating composition comprising encapsulating-microspheres, which may contain an adjuvant, where the microspheres having a diameter of 1 nm to 10 microns are comprised of: (a) a biodegradable-biocompatible poly (DL-lactide-co-glycolide) as the bulk matrix, where the copolymer (lactide to glycolide L/G) ratio for uncapped and end-capped polymer is 0/100 to 1/99; and (b) an immunogenic substance comprising a bacteria, virus, fungus, parasite, or derivative, that serves to elicit the production of antibodies in animal subjects.

USE - The biocompatible and biodegradable microspheres can provide programmable sustained release of biologically active agents, including polypeptides over a period of up to 100 days in an **aqueous** physiological environment with little or no burst release. They can be used for the delivery of e.g. insulins, AZT, diethyl silbestrol, 17-beta-oestradiol, oestron, ethinyl estradiol, mestranol, norethindrone, norgestryl, ethynodiol diacetate, lynoestrenol, medroxyprogesterone

acetate, dimethisterone, megestrol acetate, chlormadinine acetate, norgestimate, norethisterone, ethisterone, melentate, norgestimate, norethisterone, ethisterone, melentate, melengestrol, norethynodrel, nonylphenoxypolyoxyethylene **glycol**, benzethonium chloride, chlorindanol, aluminium hydroxide, calcium carbonate, magnesium carbonate, sodium carbonate, chloropromaquine HCl, clozapine, mesoridazine, metiapine, reserpine, thioridazine, chlordiazepoxide, diazepam, meprobamate, temazepam, codeine, phenobarbital, sodium pentobarbital, sodium secobarbital, testosterone, testosterone propionate, sulphonamides, 4-aminoquinolines, 8-aminoquinolines, pyrimethamine, mazindol. phentermine, L-dopa, atropine, methscopolamine bromide, dextromethorphan, noscapine, Rauwolfia alkaloids, nitroglycerin, organic nitrites, pentaerythriotetranitrate, potassium chloride, ergotamine with and without caffeine, hydrogenated ergot alkaloids, dihydroergocristine methanesulphate, dihydrooergocornine methanesulphonate, dihydroergokroyptine methanesulphate, atropine sulphate, Belladonna, hyoscine hydrobromide, dihydrocodienone, meperidine, **morphine**, salicylates, asprin, **acetaminophen**, d-propoxyphene, ceflacor, cefuroxime, chloramphenical, gentamycin, Kanamycin A, Kanamycin B, ampicillin, amoxicillin, streptomycin A, antimycin A, chloropamtheniol, metromidazole, oxytetracycline, penicillin G, minocycline, ciprofloxacin, ofoxacin, clarithromycin, frythromycin (sic), gentamicin, amikacin, tobramycin, kanamycin, ampicillin, polymyxin-B, amphotericin-B, aztrofonam, chloramphenicol, fusidans, lincosamides, metronidazole, nitro-furantion, imipenem/cilastin, quinolones, rifampin, polyenes, sulphonamides, trimethoprim, vancomycin, teicoplanin, imidazoles, mephenytoin, phenobarbital, trimethadione, triethylperazine, chlorophinazine, dimenhydrinate, diphenhydramine, perphenazine, tripelennamine, hydrocortisone, prednisolone, prednisone, allopurinol, indomethacin, phenylbutazone, prostaglandin, thiotepa, chloramucil, cyclophosphamide, melphalan, nitrogen mustard, methotrexate, aztreonam, and refampin.

Dwg.0/54

=> d bib abs 143

L43 ANSWER 1 OF 24 MEDLINE
AN 91181751 MEDLINE
DN 91181751
TI [Acute pain in children and its treatment].
La douleur aigue de l'enfant et son traitement.
AU Dalens B
CS Departement d'Anesthesie-Reanimation, Pavillon Gosselin, Hotel-Dieu, Clermont-Ferrand..
SO ANNALES FRANCAISES D ANESTHESIE ET DE REANIMATION, (1991) 10 (1) 38-61.
Ref: 200
Journal code: 4ZT. ISSN: 0750-7658.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA French
FS Priority Journals
EM 199107
AB Pain in paediatrics has long been underestimated. The numerous scientific studies carried out during the last decade show that its existence can no longer be doubted: in fact, pain already exists during the neonatal period, and probably throughout the last trimester of gestation as well. Pain pathways mature during the embryonic period and peripheral receptors develop between the 7th and 20th week. A-delta and C fibers, as well as spinal roots and nerves, are completely differentiated before the end of the second month. The development of specific neurotransmitters and thalamic and cortical dendritic branching occurs later on; it is well enough developed to allow perception of painful stimuli (slow or protopathic component) from the beginning of the foetal period onwards. The discriminative rapid component develops in parallel to myelinisation, and the psycho-affective component, which requires a long and complex learning process, will not be fully operative until the end of puberty. Assessing pain, already a difficult task in the adult, is all the more so in children because of lesser verbal communicative capabilities, difficulty in handling abstract concepts, lack of experience of painful stimuli to make comparisons, and ignorance of their body image. In the very young child, diagnosing pain relies on suggestive circumstances, and an altered behaviour, knowing that no one symptom in pathognomonic. As the child grows up, methods for self-assessment of pain become usable, such as coloured scales and simplified verbal scales. However, behavioural tests remain the mainstay until the prepubertal period. The treatment of acute pain requires a reasoned approach which takes into account the state of the child, that of the aetiological investigations, the likely course of the lesions, as well as the patient's analgesic requirements. Therapeutic means do not differ from those for adult patients; however, the differences of distribution of body **water**, the small possibilities of linking with plasma proteins, and limited conjugation with **glucuronate** must be taken into account, especially during the first months of life. Local and regional anaesthetic block techniques are of great interest in elective and emergency surgery, as well as in trauma: they can provide complete pain relief, mostly without having any effect on the patient's physiological state (haemodynamics and consciousness). Peripherally acting analgesic agents, which are well supported on the whole, as well as co-analgesics, have a great part to

play, although there are less drugs available than for adults. The most useful ones are **paracetamol**, followed by the salicylates, propionic acid derivatives and non steroid **anti-inflammatory** drugs.(ABSTRACT TRUNCATED AT 400 WORDS)

=> d bib abs l44

L44 ANSWER 1 OF 2 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 97-197200 [18] WPIDS
DNC C97-063219
TI Antipyretic and analgesic agent - comprises e.g. **ibuprofen**, oxaprozin and stevia.
DC B05
PA (TAIS) TAISHO PHARM CO LTD
CYC 1
PI JP 09052825 A 970225 (9718)* 6 pp
ADT JP 09052825 A JP 96-124372 960520
PRAI JP 95-142861 950609
AN 97-197200 [18] WPIDS
AB JP09052825 A UPAB: 970502
Antipyretic analgesic agent contains **ibuprofen**, **acetaminophen**, oxaprozin, loxoprofen, **ketoprofen** and/or fenbufen and stevia.

The combination is specifically limited to combination of stevia (sweet principle of Stevia Rebaudiana Bertoni, a Compositae family plant) and one of **ibuprofen**, **acetaminophen**, oxaprozin, loxoprofen, **ketoprofen** and fenbufen; stevia includes Stevia extract consisting of mixed or single principle of Stevia plant, e.g. stevioside, rebaudioside A, dulcoside A, dulcoside B, rebaudioside E, rebaudioside D, steviorubioside, rebaudioside B and steviol, wherein rebaudioside A is most pref.; and effective dose of stevia is 5-100, pref. 1-50, mg. per one healthy person, and e.g. 0.001-0.1, pref. 0.007-0.03 pts.wt. per 1 pt.wt. of **ibuprofen**.

USE/ADVANTAGE - The compsn. is oral prepn. of favourable taste and feeling in internal use. The compsn. is relatively **stable** to heat and acid, highly safe in use mildly sweet with less after taste, non-fermentable, and no browning at heat treatment, by the effect of coformulation with stevia.

Sample-A (liquid prepn.) was prepd. from 12 mg. bromhexine hydrochloride, 24 mg. dihydrocodeine phosphate, 90 mg. lysozyme chloride, 48 mg. noscapine, 60 mg. dl-methylephedrine hydrochloride, 7.5 mg. carbinoxamine maleate, 900 mg. **acetaminophen**, 75 mg. anhydrous caffeine, 24 mg. vitamin B1 nitrate, 12 mg. vitamin B2, 15 mg. stevia, D-**sorbitol** soln., benzoic acid, sodium citrate, polyoxyethylene hardened castor oil and distilled **water** (to adjust to 60 ml.); and sample-B was similarly prepd. without using stevia.
Dwg.0/3

=> d bib abs l44 2

L44 ANSWER 2 OF 2 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 93-260298 [33] WPIDS
DNC C93-115532
TI **Aq**. pharmaceutical suspension suitable for admin. to paediatric or geriatric patients - comprises active agent e.g. **acetaminophen**, a suspension of xanthan gum and microcrystalline cellulose, **water** and opt. sweetener.
DC B05 B07
IN BLASE, C M; SHAH, M N
PA (MCNI) MCNEIL-PPC INC
CYC 11
PI EP 556057 A1 930818 (9333)* EN 11 pp
R: BE CH ES FR GB IT LI NL
AU 9332924 A 930819 (9340)
CA 2089430 A 930815 (9345)
US 5272137 A 931221 (9351) 7 pp
US 5409907 A 950425 (9522) 7 pp
EP 556057 B1 961009 (9645) EN 12 pp
R: BE CH ES FR GB IT LI NL
AU 671610 B 960905 (9647)
ES 2095566 T3 970216 (9714)
CA 2089430 C 980421 (9827)
ADT EP 556057 A1 EP 93-301018 930212; AU 9332924 A AU 93-32924 930209; CA 2089430 A CA 93-2089430 930212; US 5272137 A US 92-835877 920214; US 5409907 A Cont of US 92-835877 920214, US 93-168605 931216; EP 556057 B1 EP 93-301018 930212; AU 671610 B AU 93-32924 930209; ES 2095566 T3 EP 93-301018 930212; CA 2089430 C CA 93-2089430 930212
FDT US 5409907 A Cont of US 5272137; AU 671610 B Previous Publ. AU 9332924;
ES
2095566 T3 Based on EP 556057
PRAI US 92-835877 920214; US 93-168605 931216
AN 93-260298 [33] WPIDS
AB EP 556057 A UPAB: 931119
Pharmaceutical suspension comprises: (a) a pharmaceutical active agent; (b) a suspending system consisting of a xanthan gum (as suspension stabiliser) (0.12-0.2g per 100ml of suspension), and microcrystalline cellulose (0.6-1.0g per 100ml of suspension); (c) **water**; and opt. (d) a sweetening agent and a flavouring agent.
Pref. the active agent is **acetaminophen**, **ibuprofen**, famotadine, pseudoephedrine, hydrochloride, chlorpheniramine maleate, astemizole, dextrmethorphan hydrobromide, guaifenesin, etc.. The sweetening agent is xylose, ribose, **glucose**, mannose, galactose, **fructose**, dextrose, **sucrose**, maltose, partially hydrolysed starch solids, etc..
USE/ADVANTAGE - The suspensions are esp. useful for admin. of drugs to children and geriatric patients who have difficulty swallowing tablets or capsules. They are expected to achieve higher patient compliance. The solns. are **stable**, pourable and have a pleasant taste.
Dwg.0/0
ABEQ US 5272137 A UPAB: 940209
Pharmaceutical suspension comprises (a) **acetaminophen**, famotidine, pseudoephadrine hydrochloride, chlorpheniramine maleate, asterizole, dextromethorphanhydrobromide, quai/enesin, diphenyl dramine hydrochloride, loperamide hydrochloride, simethicone and/or antacids; (b) a suspending system comprising 0.12-0.2g/100 me xanthan gum; and

0.5-1g/100 ml microcyrstalline cellulose, (c) **water**; and (d) a sweetening agent and a flavouring agent.

USE/ADVANTAGE - The taste of the compsn. is masked and the compsn. may be admininstered orally as a palatable liq. dosage form even for paediatric applications.

Dwg.0/0

ABEQ US 5409907 A UPAB: 950609

Pharmaceutical suspension comprises (a) **acetaminophen**, famotidine, pseudoephedrine hydrochloride, chlorpheniramine maleate, astemizole, dextromethorphan hydrobromide, gualfenesin, diphenhydramine hydrochloride, loperamide hydrochloride, simethicone and/or antacids; (b) a suspending system comprising a stabilising amt. of xanthan gum and microcrystalline cellulose; (c) **water** and (d) a sweetening agent and a flavouring agent to provide a palatable taste. Sweetening agent is e.g. xylose, ribose, **glucose**, mannose, **fructose**, galactose glycerin, saccharin and/or aspartame etc.

ADVANTAGE - Compsn. remains in solid form and is less likely to be tasted while in the mouth, since reduced amts. of **water** are involved. Compsn. is physiochemically **stable** and is esp. suited for geriatric or pediatric applicns.

Dwg.0/0

ABEQ EP 556057 B UPAB: 961111

A pharmaceutical suspension comprising: a therapeutic amount of a pharmaceutical active; a suspending system consisting essentially of a suspension stabilizing effective amount of xanthan gum in the range of 0.1 to 0.2 grams per 100 mL of the suspension and microcrystalline cellulose in the range of 0.5 to 1.0 grams per 100 mL of the suspension; **water**; and an effective amount of a sweetening agent and a flavouring agent to provide a palatable taste to said pharmaceutical suspension.

Dwg.0/0

=> d bib abs l45

L45 ANSWER 1 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 97-197200 [18] WPIDS
DNC C97-063219
TI Antipyretic and analgesic agent - comprises e.g. **ibuprofen**, oxaprozin and stevia.
DC B05
PA (TAIS) TAISHO PHARM CO LTD
CYC 1
PI JP 09052825 A 970225 (9718)* 6 pp
ADT JP 09052825 A JP 96-124372 960520
PRAI JP 95-142861 950609
AN 97-197200 [18] WPIDS
AB JP09052825 A UPAB: 970502
Antipyretic analgesic agent contains **ibuprofen**, **acetaminophen**, oxaprozin, loxoprofen, **ketoprofen** and/or fenbufen and stevia.

The combination is specifically limited to combination of stevia (sweet principle of Stevia Rebaudiana Bertoni, a Compositae family plant) and one of **ibuprofen**, **acetaminophen**, oxaprozin, loxoprofen, **ketoprofen** and fenbufen; stevia includes Stevia extract consisting of mixed or single principle of Stevia plant, e.g. stevioside, rebaudioside A, dulcoside A, dulcoside B, rebaudioside E, rebaudioside D, steviorubioside, rebaudioside B and steviol, wherein rebaudioside A is most pref.; and effective dose of stevia is 5-100, pref. 1-50, mg. per one healthy person, and e.g. 0.001-0.1, pref. 0.007-0.03 pts.wt. per 1 pt.wt. of **ibuprofen**.

USE/ADVANTAGE - The compsn. is oral prepn. of favourable taste and feeling in internal use. The compsn. is relatively stable to heat and acid, highly safe in use mildly sweet with less after taste, non-fermentable, and no browning at heat treatment, by the effect of coformulation with stevia.

Sample-A (liquid prepn.) was prepd. from 12 mg. bromhexine hydrochloride, 24 mg. dihydrocodeine phosphate, 90 mg. lysozyme chloride, 48 mg. noscapine, 60 mg. dl-methylephedrine hydrochloride, 7.5 mg. carbinoxamine maleate, 900 mg. **acetaminophen**, 75 mg. anhydrous caffeine, 24 mg. vitamin B1 nitrate, 12 mg. vitamin B2, 15 mg. stevia, D-**sorbitol** soln., benzoic acid, sodium citrate, polyoxyethylene hardened castor oil and distilled **water** (to adjust to 60 ml.); and sample-B was similarly prepd. without using stevia.
Dwg.0/3

=> d bib abs l45 2-4

L45 ANSWER 2 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 96-371107 [37] WPIDS
DNC C96-117683
TI Taste-masking liquid excipient base - for disguising taste of pharmaceutically active cpds. comprises polyethylene **glycol** and a cellulosic cpd..
DC A11 A25 A96 B05 B07
IN GO, Z O; POPLI, S D; GO, Z; POPLI, S; DASS POPLI, S; ONG GO, Z
PA (AMHP) AMERICAN HOME PROD CORP
CYC 71
PI WO 9623486 A1 960808 (9637)* EN 29 pp
RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
AU 9647576 A 960821 (9648)
US 5616621 A 970401 (9719) 8 pp
NO 9703480 A 970929 (9750)
EP 806939 A1 971119 (9751) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
FI 9703147 A 970929 (9751)
BR 9606863 A 971223 (9806)
MX 9705724 A1 971101 (9902)
AU 698718 B 981105 (9905)
NZ 302009 A 981223 (9906)
ADT WO 9623486 A1 WO 96-US577 960116; AU 9647576 A AU 96-47576 960116; US 5616621 A US 95-380540 950130; NO 9703480 A WO 96-US577 960116, NO 97-3480
970729; EP 806939 A1 EP 96-903512 960116, WO 96-US577 960116; FI 9703147 A
WO 96-US577 960116, FI 97-3147 970729; BR 9606863 A BR 96-6863 960116, WO 96-US577 960116; MX 9705724 A1 MX 97-5724 970729; AU 698718 B AU 96-47576 960116; NZ 302009 A NZ 96-302009 960116, WO 96-US577 960116
FDT AU 9647576 A Based on WO 9623486; EP 806939 A1 Based on WO 9623486; BR 9606863 A Based on WO 9623486; AU 698718 B Previous Publ. AU 9647576, Based on WO 9623486; NZ 302009 A Based on WO 9623486
PRAI US 95-380540 950130
AN 96-371107 [37] WPIDS
AB WO 9623486 A UPAB: 960918
Taste-masking liquid excipient base, for admin. of relatively large amts. of unpleasant tasting pharmaceutically active cpds., comprises: (a) polyethylene **glycol** having a mol. wt. of 950-2200; and (b) a cellulosic cpd. The spindle viscosity of the liquid excipient base is 150-1000 centipoises at 50rpm, and 150-1200 centipoises at 10rpm.
USE - The excipient base may be used to mask the taste of, e.g., antihistamines, decongestants, antitussives, expectorants, **NSAIDs** or analgesics, esp. chlorpheniramine, brompheniramine, dexchlorpheniramine, dexbrompheniramine, triprolidine, diphenhydramine, doxylamine, tripelennamine, cyproheptatine, bromo-diphenhydramine, phenindamine, pyrilamine, azatadine, pseudoephedrine HCl, phenylpropanolamine, phenylephrine, oterpin hydrate, guaifenesin, potassium iodide, potassium citrate, potassium guaicol-sulphonate, caramiphen, codeine phosphate, codeine sulphate, dextromethorphan HBr, propionic acid derivs., acetic acid derivs., fenamic acid derivs.,

biphenylcarboxylic acid derivs., oxicams, **ibuprofen**, **ketoprofen**, naproxen or **acetaminophen**.

ADVANTAGE - The excipient base allows taste-masking of high dosage amts. of unpleasant tasting medicines in small amts. of vehicle.

Dwg.0/0

ABEQ US 5616621 A UPAB: 970512

A pharmaceutical composition comprising (i) a liquid excipient base consisting essentially of **water** and per 100 millilitres of said base about 5 to about 20 grams of a (a) polyethylene **glycol** having a molecular weight of about 950 to about 2200, and (b) a cellulosic compound selected from the group consisting of methyl cellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyethyl methylcellulose, hydroxypropyl methylcellulose, carboxymethyl cellulose, mixtures and salts thereof, the weight ratio of said polyethylene **glycol** to said cellulosic compound being between about 100:1 and about 20:1, and the spindle viscosity of the liquid excipient base being between about 150 and about 1000 centipoises at 50 RPM and 150-1200 centipoises at 10 RPM, and (ii) at least one pharmaceutically active compound selected from the group consisting of antihistamines, decongestants, antitussives, expectorants, non-steroidal **anti-inflammatory** drugs (**NSAIDs**) and analgesic drugs, said pharmaceutically active compound being dissolved in the liquid excipient base.

Dwg.0/0

L45 ANSWER 3 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 94-357868 [44] WPIDS
DNC C94-163249
TI Pharmaceutical compsn. for filling soft gelatin shells - obtd. by mixing drugs with solvent system contg. polyvinyl pyrrolidone and tri. ester.
DC A96 B07
IN WHITE, R K
PA (PROC) PROCTER & GAMBLE CO
CYC 2
PI WO 9425008 A1 941110 (9444)* EN 24 pp
US 5431916 A 950711 (9533) 8 pp
JP 08509498 W 961008 (9705) 26 pp
ADT WO 9425008 A1 WO 94-US3753 940406; US 5431916 A US 93-54762 930429; JP 08509498 W JP 94-524280 940406, WO 94-US3753 940406
FDT JP 08509498 W Based on WO 9425008
PRAI US 93-54762 930429
AN 94-357868 [44] WPIDS
AB WO 9425008 A UPAB: 941223

Prepn. of a pharmaceutical compsn. (I) comprises (a) combining, mixing and heating a first component contg. a safe and effective amt. (pref. 10-50%) of polyvinyl pyrrolidone (PVP) having mol.wt. 5000-25000 and (novel feature) a safe and effective amt. (pref. 10-50%) of a triester (TE) contg. a safe and effective amt. (pref. 0.01-50%) of at least one pharmaceutical active; and (b) admixing the first component with a second component contg. a safe and effective amt. of a second pharmaceutical active (pref. with heating). The TE:PVP ratio is 2.0:0.5 to 1:0:1.0.

PREFERRED COMPOSITIONS- TE is a one or more of triethyl citrate, glyceryl triacetate, acetyltriethyl citrate and acetyltri-n-butyl citrate.

The pharmaceutical active is one or more of antitussives, antinauseants, nutritional supplements, laxatives, appetite suppressants, analgesics, antiasthmatics, antihistamines, decongestants, xanthines, expectorants,

antacids, antidiarrhoeals and H2-receptor antagonists, esp. at least one analgesic selected from **acetaminophen**, acetylsalicylic acid, **ketoprofen**, **fenoprofen**, flurbiprofen, **ibuprofen** and naproxen. The components opt. also include (i) 0.1-20% **water** and/or polyethylene **glycol**; (ii) 0.1-10% surfactant; and/or (iii) a further pharmaceutical active selected from the same activity categories as above, pref. **acetaminophen**, dextromethorphan, pseudoephedrine, doxylamine or chlorpheniramine.

USE - (I) is esp. encapsulated in a soft gelatin shell (claimed) for oral admin.

ADVANTAGE - The PVP/TE solvent system has good solvating properties, and is capable of dissolving relatively large amts. of a wide range of pharmaceutical actives for oral admin., including acidic cpds. such as non-steroidal **antiinflammatories**. The PVP/TE system is a non-solvent for **glycerol** and other plasticisers for soft gelatin capsules, and thus facilitates selection of plasticisers and prevents migration of plasticiser from the shell into the filling (by forming a barrier). The **water** tolerance of TE allows incorporation of additional **water**-soluble actives, expanding the range of activity of a single compsn.

Dwg.0/0

ABEQ US 5431916 A UPAB: 950824

Encapsulated pharmaceutical compsn. comprises (i) a triester, (ii) at least one analgesic, **antiinflammatory**, antipyretic, calcium channel blocker, beta blocker, antibacterial, antidepressant, antidiabetic, antiemetic, antihistamine, cerebral stimulant, sedative, antiparasitic, expectorant, diuretic, decongestant, antitussive, muscle relaxants, anti-Parkinsonian agent, bronchodilators, cardiotonics, antibiotics, antivirals and/or nutritional supplements or their salts, (iii) polyvinylpyrrolidone and (iv) an oral carrier, the ratio of (i):(iii) is 2-0.05 to 1-1.0.

ADVANTAGE - (i) has low **water** tolerance allowing for the inclusion of additional **water** soluble pharmaceuticals, expanding the range of activity of a single compsn.

Dwg.0/0

L45 ANSWER 4 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 93-259193 [33] WPIDS
DNC C93-115104
TI Compsn. for dissolution in hot **water** for treating colds and influenza - contains an analgesic, an antihistamine, an antitussive, a decongestant, citric acid, bi carbonate and calcium carbonate.
DC B05
IN PANDYA, H B
PA (MILE) MILES INC
CYC 1
PI CA 2084028 A 930528 (9333)* 12 pp
ADT CA 2084028 A CA 92-2084028 921127
PRAI US 91-799033 911127
AN 93-259193 [33] WPIDS
AB CA 2084028 A UPAB: 931119

A compsn. for dissolution in hot **water**, for treating cold and flu symptoms compries, as wt.%: a) 0.9-17% analgesic selected from **acetaminophen**, acetylsalicylic acid, **ketoprofen** and **ibuprofen**; b) 0.07-0.14% antihistamine; c) 0.4-1.2% antitussive; d) 1-2% decongestant; e) 10-20% citric acid; f) 1.5-2.2% Na or KHCO3; g) 1.5-3% CaCO3; h) 2-4% flavours and sweeteners; i) 1.5-2.5% tablet lubricants; and j) further tabletting aids.

The antihistamine is e.g. chlorpheniramine maleate, brompheniramine

maleate or pyrilamine maleate. The antitussive is e.g. dextromethorphan hydrobromide, and the decongestant is phenylpropanolamine tartrate or bitartrate, phenylephrine bitartrate or pseudoephedrine sulphate or the corresp. HCl salts. Tabletting aids include inert fillers or binders, partic. **mannitol**. Polyvinyl pyrrolidone, organopolysiloxane or dioctyl sodium sulphosuccinate surfactants may be included.

USE/ADVANTAGE - The new compsn. is an effervescent tablet for dissolution in hot **water**, without the conventional use of **sugar** and without glycine. The bitter taste of e.g. **acetaminophen** is masked by CaCO3.

Dwg.0/0

=> d bib abs l51 1-4

L51 ANSWER 1 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 95102648 EMBASE
DN 1995102648
TI The effects of oral droperidol versus oral metoclopramide versus both oral droperidol and metoclopramide on postoperative vomiting when used as a premedicant for strabismus surgery.
AU Kymer P.J.; Brown Jr. R.E.; Lawhorn C.D.; Jones E.; Pearce L.
CS Division of Pediatric Anesthesia, Arkansas Children's Hospital, 800 Marshall Street,Little Rock, AR 72202-3591, United States
SO Journal of Clinical Anesthesia, (1995) 7/1 (35-39).
ISSN: 0952-8180 CODEN: JCLBE7
CY United States
DT Journal; Article
FS 009 Surgery
024 Anesthesiology
037 Drug Literature Index
LA English
SL English
AB Study Objective: To compare the efficacy of oral droperidol versus oral metoclopramide, or both oral droperidol and metoclopramide, on postoperative vomiting when used as a premedicant for strabismus surgery. Design: Double- blind, randomized, prospective study. Setting: Academic children's hospital. Patients: 154 ASA physical status I and II ambulatory patients, ages 1 to 15 years, scheduled for strabismus surgery. Interventions: Patients were randomly assigned to receive colored **sugar water** containing either droperidol 300 mcg/kg orally, metoclopramide 0.15 mg/kg orally, both droperidol 300 mcg/kg and metoclopramide 0.15 mg/kg orally, or no active ingredient (placebo group) as a premedicant. The premedications were given orally 1 to 1.5 hours prior to the operation. Measurements and Main Results: Patients were analyzed for the number of episodes of vomiting from the time of their emergence from anesthesia through the first 24 hours postoperatively, including the convalescent period at home. Patients were also analyzed for length of hospital stay. There were no statistically significant differences between groups regarding age, premedication time, surgery time, or discharge time. Droperidol and droperidol-metoclopramide were significantly more effective ($p < 0.012$) than either the metoclopramide group or the placebo group in preventing postoperative nausea and vomiting following strabismus surgery. Conclusions: Our data suggest that oral droperidol 300 mcg/kg and the combination of oral droperidol 300 mcg/kg and metoclopramide 0.15 mg/kg are effective in reducing the frequency of vomiting within the first 24 hours after strabismus surgery. The combination of oral droperidol and oral metoclopramide is highly effective in reducing the frequency of vomiting postoperatively in strabismus ambulatory surgery patients ($p = 0.017$). This combination seems to represent an inexpensive alternative to the more costly **ondansetron.**

L51 ANSWER 2 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 74185907 EMBASE
DN 1974185907

TI The use of diamorphine in the management of terminal cancer.
AU Twycross R.G.
CS St Christopher's Hosp., London, United Kingdom
SO J.THANATOLOGY, (1972) 2/3-4 (733-743).
CODEN: JTHNA2
DT Journal
FS 037 Drug Literature Index
020 Gerontology and Geriatrics
006 Internal Medicine
016 Cancer
009 Surgery
LA English
AB Although the majority of patients with pain problems at St. Christopher's and St. Joseph's receive diamorphine there is a minority who are maintained on a variety of other analgesics ranging from aspirin and **paracetamol** to dextropropoxyphene and the synthetic narcotics such as pentazocine and phenazocine. Of the majority who receive diamorphine, only 15% have it by injection throughout their time in hospital. The remainder take it as an oral mixture consisting of diamorphine 2.5 mg or more, cocaine 10 mg, ethyl alcohol (95%) 2.5 ml, syrup (66% **sucrose** in **water**) 5 ml, made up to 20 ml by the addition of chloroform **water**. These patients are maintained on a suitable dose given regularly every 4 hr to prevent the recurrence of pain. The right dose is that dose which keeps the patient free of pain. With the aid of a night sedative most patients do not require a 2:00 a.m. dose. A tradition has developed whereby almost all patients receive a phenothiazine syrup with the diamorphine mixture, usually either **prochlorperazine** or chlorpromazine. Originally given to relieve coexistent nausea or vomiting, it is now also given to mask the bitter taste of diamorphine. Unfortunately, just over 1% of the patients admitted with severe pain fail to obtain adequate relief, and a further 20%, although much relieved, do experience pain from time to time especially when moved.

L51 ANSWER 3 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 92-403369 [49] WPIDS
DNC C92-179143
TI Coated prepn, avoiding drug elution and bitterness - prepd. by granulating agent contg. medical cpd., wax- and **water** swelling substances and heat treating for surface coating.
DC B02 B07
PA (SHIO) SHIONOGI & CO LTD
CYC 1
PI JP 04300821 A 921023 (9249)* 6 pp
ADT JP 04300821 A JP 91-66563 910329
PRAI JP 91-66563 910329
AN 92-403369 [49] WPIDS
AB JP04300821 A UPAB: 931116
Prepn. comprises (i) dry granulating agent contg. medical cpd. (less than 40 wt.%, (less than 25 wt.%), wax substance (10-50 wt.%, (15-40 wt.%) and **water** swelling substance (5-35 wt.%, (10-35 wt.%); and (ii) heat treating to coat surface.

Pref., the prepn. can be used for medical cpd. which has unpleasant flavour or low solvent resistance property. Prepn. is coated fine granules. Medical cpd. is (+) - (6R, 7R)-7- ((Z)-2-(2-amino -4-thiazolyl) -2-penten-amide) -3-carbamoyloxymethyl -8-oxy-5- thia-1-azabicyclo

(4.2.0.) oct-2-end-2-carboxylic acid pivaloyloxymethyl ester hydrochloride.

Solvent is, e.g., **water**, ethanol, isopropanol, dichloromethane and propylene **glycol**. Medical cpd. is, e.g., flucloxacillin sodium salt, talampicillin hydrochloride, sultamycillin tosylate, and bacampicillin hydrochloride, cefaclor, cefpodoxime proxteil, cefotiumhexetil, S-1108 and cefterm pivoxil; erythromycin; lomefloxacin, norfloxacin, ofloxacin, enoxacin, pipemidic acid; dextromethorphan hydrobromide, **acetaminophen**, ketoprophen and tolfenamic acid; diphenydramin and **promethazine** hydrochloride; and dicethiamine hydrochloride. Wax substance is, e.g., hardened oil, e.g., hard castor-, hard soy-bean or hard rapeseed oil; higher alcohol, e.g., stearyl alcohol or cetanol; higher fatty acid, e.g., stearic or palmitic-acid; plant or animal fat or wax, e.g., carnauba wax, beef tallow; polyethylene **glycol**, e.g., macrogol 4000, or macrogol 6000. **Water** swelling substance is, e.g., cellulose deriv., e.g., carboxymethylcellulose calcium carboxymethylcellulose sodium (bridged CMC-Na), or lower substd. hdyroxypropyl cellulose (L-HPC); various starches, e.g., partial alpha-starch (PCS) or carboxymethyl starch-sodium (CMS-Na). Heating process is at more than 40 deg.C for 10-90 mins., (20-60 mins). Pref., wax substance melts at 40-90 deg.C (50-85 deg.C).

USE/ADVANTAGE - Coats medical cpd. which is easily decomposed or denatured by solvent, e.g., **water** and organic solvent.

Dwg.0/0

L51 ANSWER 4 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 87-079617 [11] WPIDS
DNC C87-033219
TI Compsn. for treating symptoms of excessive alcohol intake - comprises analgesic and nicotinamide or nicotinamide adenine di nucleotide.
DC B05
PA (BLAS-I) BLASS D H
CYC 16
PI WO 8701285 A 870312 (8711)* EN 31 pp
RW: AT BE CH DE FR GB IT
W: AU BR DK FI
AU 8662877 A 870324 (8723)
EP 271489 A 880622 (8825) EN 11 pp
R: AT BE CH DE FR GB IT LI LU NL SE
FI 8800714 A 880216 (8844)
EP 271489 B 900228 (9009) EN
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3669105 G 900405 (9015)
US 5053396 A 911001 (9142)#
ADT WO 8701285 A WO 86-EP492 860821; EP 271489 A EP 86-904826 860821; US 5053396 A US 90-562425 900801
PRAI GB 85-21275 850827; WO 85-EP492 850821
AN 87-079617 [11] WPIDS
AB WO 8701285 A UPAB: 930922
Therapeutic compsn. for treating the symptoms associated with excessive intake of an alcohol comprises (a) an analgesic(s); (b) at least 7% of nicotinamide and/or nictoin-amide adenine dinucleotide (NAD).

The compsn. pref. also contains a **water**-soluble vitamin(s), an antacid, an electrolyte salt replacing component, trace metal ions, an antihistamine(s), **fructose** and an alkaloid having a stimulating effect.

USE/ADVANTAGE - The comosn. is useful for treating acute and/or

chronic symptoms associated with excessive ingestion or inhalation of alcohols, esp. of EtOH in alcoholic beverages. The nicotinamide and/or NAD may aid the breakdown of alcohol and the prods. formed from it in the body, and it may also protect tissues against their toxic effects. Also NAD or its precursor has a generally restorative and invigorating effect on the body and accelerates alcohol breakdown, while protecting tissues against the toxic effects of the alcohol and its breakdown prods.

Ther is also a synergistic action between the components of the compsn., and this is increased when certain **water**-soluble vitamins are present.

0/0

ABEQ EP 271489 B UPAB: 930922

A therapeutic compsn for the treatment of the symptoms associated with the excessive intake of alcohol, comprising: (a) at least one analgesic; (b) 70 to 1500 mg per unit dose of nicotinamide and/or 70 to 300 mg of nicotinamide adenine dinucleotide (NAD); the amt of component (b) being at least 7%, pref 10% and most pref considerably over 10% by weight of component (a) with the proviso that if component (a) is acetylsalicyclic acid, this cpd is present in an amt of 300 to 1000 mg per unit dose and that the amt of component (b) is at least 10% and less than 100 % by weight of the amt of component (a); and further opt comprising one or more of the following components; (c) at least one additional **water** soluble vitamin; (d) an antacid component; (e) an electrolyte salt replacing component; (f) trace metal ions; (g) at least one antihistamine; (h) **fructose**; (i) at least one alkaloid having a stimulating effect; (j) usual additives according to the form of administration, like sweetening agents, flavouring agents, colouring agents effervescent components, carriers or fillers.

ABEQ US 5053396 A UPAB: 930922

The compsn. contains:- (a) an analgesic and (b) 70-1500 mg per unit does of nicotinamide (I) or 70-300 mg of nicotinamide adenine dinucleotide (NAD). The amount of (b) is at least 7 wt.% of (a). The compsn. also contains one or more of the following: (c) a **water**-soluble vitamin selected from pantothenic acid, riboflavin, pyridoxine hydrochloride, thiamine hydrochloride and ascorbic acid; (d) an antacid component; (e) a component htat that replaces electrolyte salts; (f) trace metal ions; (g) an antihistamine selected form **promethazine** hydrochloride; chlor-phenisamine maleate; diphenhydramine hydrochloride; dimenhydrinate; carboxamine maleate, pyrilamine maleate; tripelennamine hydrochloride or lactate; **meclizine** hydrochloride or buclizine hydrocchloride; h) **fructose**; (i) an alkaloid stimulant; and (j) sweetening agents, flavourings, colours, effervescent components, carriers and/or fillers as appropriate. The analgesic is diflunisal, sulindac, fenoprofen calcium, **acetaminophen**, mefenamic acid, naproxen, codeine, dextropropoxyphene HCl or meperidine.

USE/ADVANTAGE - The compsn. can be used to treat acute or chronic symptoms, including hangovers, alcoholic polyneuritis, tremors, muscle weakness and loss of coordination. It is non-addictive. Dose varies, but a typical oral 'morning after' compsn. (intended for 1000 doses and consisting of soluble power or tables) contains the following: acetylsalicylic acid (900g); nicotinamide (500g); NaHCO3 (1176g); KHCO3 (1400g); citric acid (2100g); **fructose** (5000g) and

=> d bib abs l55 1-19

L55 ANSWER 1 OF 19 MEDLINE
AN 86123807 MEDLINE
DN 86123807
TI Effects of **acetaminophen** on cadmium metabolism in mice.
AU Gale G R; Atkins L M; Smith A B; Walker E M Jr; Fody E P
NC IGA V101 (134A)P-77014
SO TOXICOLOGY AND APPLIED PHARMACOLOGY, (1986 Feb) 82 (2) 368-77.
Journal code: VWO. ISSN: 0041-008X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198605
AB **Acetaminophen** (ACM) administration to mice of the (C57BL/6 X DBA/2)F1 strain produced a typical hepatic centrilobular necrosis similar to that observed in rodents and humans. To determine the effects of this drug-induced necrosis on cadmium (Cd) metabolism, mice were given a sublethal dose of CdCl2 . 2.5 **H2O** containing 109CdCl2 and maintained for a period of time sufficient for Cd-metallothionein (Cd-MT) to be synthesized and distributed. Subsequent administration of ACM ip or po evoked a marked redistribution of Cd from livers to kidneys of mice, and increased the amount of Cd excreted in urine and feces. There were only minimal or no effects on Cd concentrations in other organs assessed. The effect of ACM on Cd redistribution was antagonized by administration of cysteine, a glutathione precursor, and was enhanced by pretreatment with **phenobarbital**, a potent inducer of the cytochrome P-450 mixed-function oxidase system. Pretreatment of mice with ACM 6 or 24 hr prior to Cd administration caused aberrations of the normal Cd distribution pattern, but no effect was noted when Cd administration was delayed for 48 hr after ACM injection, indicating recovery of the mechanisms of Cd-MT synthesis and sequestration. Sephadex G-75 gel filtration chromatography of serum from ACM-treated mice showed that most of the Cd was associated with high-molecular-weight proteins, and only a minor portion was present as Cd-MT. Cd excreted in urine was predominantly in a low-molecular-weight form, but there was evidence of two minor components of higher molecular weight, neither of which eluted as Cd-MT. Cd excreted in feces was insoluble following homogenization in 0.25 M **sucrose** solution. Cd in livers and kidneys of ACM-treated mice eluted as Cd-MT. It was concluded that persons who have a moderately high Cd burden may be at risk of Cd nephrotoxicity if they incur hepatic necrosis subsequent to ACM abuse.

L55 ANSWER 2 OF 19 MEDLINE
AN 85278487 MEDLINE
DN 85278487
TI Effects of **phenobarbital**, phorone and carbon tetrachloride pretreatment on the biliary excretion of **acetaminophen** in rats.
AU Loeser W; Siegers C P
SO ARCHIVES INTERNATIONALES DE PHARMACODYNAMIE ET DE THERAPIE, (1985 Jun) 275
(2) 180-8.
Journal code: 7EK. ISSN: 0003-9780.
CY Belgium
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 198511
AB Rats with cannulated bile ducts excreted 24.6% of an i.v. dose of 100 mg/kg **acetaminophen** (AA) into bile within 8 hr, 0.9% as unchanged drug, 5.5% as sulfate, 15.1% as **glucuronide** and 3.1% as the glutathione conjugate. Pretreatment with **phenobarbital** (0.1% solution for 7 days instead of drinking **water**) significantly decreased the amount of total AA recovered in bile, to 12.8% mainly as a consequence of reduced **glucuronide** excretion (3.5%), whereas the GSH-conjugate was augmented to 6.3%. Pretreatment with the GSH-depletor phorone (250 mg/kg i.p. 1 hr prior to AA) slightly reduced the total recovery of AA to 19.2%, due to a diminished excretion of the **glucuronide** (10.3%). Liver damage due to carbon tetrachloride administration (0.5 ml/kg p.o. 24 hr prior to AA) markedly decreased the total recovery of AA to 8.9% as a consequence of the reduction of the **glucuronic** acid (5.0%) and the GSH-conjugates (0.2%). These observations are discussed with respect to the effects of **phenobarbital**, phorone and CCl4 on microsomal and cytosolic GSH-dependent enzymes involved in the metabolism of AA.

L55 ANSWER 3 OF 19 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1986:216101 BIOSIS
DN BA81:107401
TI EFFECTS OF **ACETAMINOPHEN** ON CADMIUM METABOLISM IN MICE.
AU GALE G R; ATKINS L M; SMITH A B; WALKER E M JR; FODY E P
CS VA MEDICAL CENTER, 109 BEE STREET, CHARLESTON, S.C., 29403.
SO TOXICOL APPL PHARMACOL, (1986) 82 (2), 368-377.
CODEN: TXAPA9. ISSN: 0041-008X.
FS BA; OLD
LA English
AB **Acetaminophen** (ACM) administration to mice of the (C57BL/6 .times. DBA/2)F1 strain produced a typical hepatic centrilobular necrosis similar to that observed in rodents and humans. To determine the effects of this drug-induced necrosis on cadmium (Cd) metabolism, mice were given a sublethal dose of CdCl2 .cntdot. 2.5 **H2O** containing 109CdCl2 and maintained for a period of time sufficient for Cd-metallothionein (Cd-MT) to be synthesized and distributed. Subsequent administration of ACM ip or po evoked a marked redistribution of Cd from livers to kidneys of mice, and increased the amount of Cd excreted in urine and feces. There were only minimal or no effects on Cd concentrations in other organs assessed. The effect of ACM on Cd redistribution was antagonized by administration of cysteine, a glutathione precursor, and was enhanced by pretreatment with **phenobarbital**, a potent inducer of the cytochrome P-450 mixed-function oxidase system. Pretreatment of mice with ACM 6 or 24 hr prior to Cd administration caused aberrations of the normal Cd distribution pattern, but no effect was noted when Cd administration was delayed for 48 hr after ACM injection, indicating recovery of the mechanisms of Cd-MT synthesis and sequestration. Sephadex G-75 gel filtration chromatography of serum from ACM-treated mice showed that most of the Cd was associated with high-molecular-weight proteins, and only a minor portion was present as Cd-MT. Cd excreted in urine was predominantly in a low-molecular-weight form, but there was evidence of two minor components of higher molecular weight, neither of which eluted as Cd-MT, Cd excreted in feces was insoluble following homogenization in 0.25 M **sucrose** solution. Cd in livers and kidneys of ACM-treated mice

eluted as Cd-MT. It was concluded that persons who have a moderately high Cd burden may be at risk of Cd nephrotoxicity if they incur hepatic necrosis subsequent to ACM abuse.

L55 ANSWER 4 OF 19 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1985:428502 BIOSIS
DN BA80:98494
TI EFFECTS OF **PHENOBARBITAL** PHORONE AND CARBON TETRACHLORIDE PRETREATMENT ON THE BILIARY EXCRETION OF **ACETAMINOPHEN** IN RATS.
AU LOESER W; SIEGERS C-P
CS INST. TOXIKOLOGIE, MED. HOCHSCHULE LUEBECK, RATZEBURGER ALLEE 160, D-2400 LUEBECK, FRG.
SO ARCH INT PHARMACODYN THER, (1985) 275 (2), 180-188.
CODEN: AIPTAK. ISSN: 0003-9780.
FS BA; OLD
LA English
AB Rats with cannulated bile ducts excreted 24.6% of an i.v. dose of 100 mg/kg **acetaminophen** (AA) [analgesic] into bile within 8 h, 0.9% as unchanged drug, 5.5% as sulfate, 15.1% as **glucuronide** and 3.1% as the glutathione conjugate. Pretreatment with **phenobarbital** (0.1% solution for 7 days instead of drinking **water**) significantly decreased the amount of total AA recovered in bile, to 12.8% mainly as a consequence of reduced **glucuronide** excretion (3.5%) whereas the GSH-conjugate was augmented to 6.3%. Pretreatment with the GSH-depletor phorone (250 mg/kg i.p. 1 h prior to AA) slightly reduced the total recovery of AA to 19.2%, due to a diminished excretion of the **glucuronide** (10.3%). Liver damage due to CCl4 administration (0.5 mg/kg p.o. [per os] 24 h prior to AA) markedly decreased the total recovery of AA to 8.9% as a consequence of the reduction of the **glucuronic** acid (5.0%) and the GSH-conjugates (0.2%). The effects of **phenobarbital**, phorone and CCl4 on microsomal and cytosolic GSH-dependent enzymes involved in the metabolism of AA are discussed.

L55 ANSWER 5 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 94126267 EMBASE
DN 1994126267
TI Human acute toxicity prediction of the first 50 meic chemicals by a battery of ecotoxicological tests and physicochemical properties.
AU Calleja M.C.; Persoone G.; Geladi P.
CS Research Group for Chemometrics, Institute of Chemistry, University of Umea,Umea, Sweden
SO Food and Chemical Toxicology, (1994) 32/2 (173-187).
ISSN: 0278-6915 CODEN: FCTOD7
CY United Kingdom
DT Journal; Article
FS 046 Environmental Health and Pollution Control
052 Toxicology
037 Drug Literature Index
LA English
SL English
AB Five acute bioassays consisting of three cyst-based tests (with Artemia salina, Streptocephalus proboscideus and Brachionus calyciflorus), the Daphnia magna test and the bacterial luminescence inhibition test (Photobacterium phosphoreum) are used to determine the acute toxicity of the 50 priority chemicals of the Multicentre Evaluation of In Vitro Cytotoxicity (MEIC) programme. These tests and five physicochemical properties (n-octanol- **water** partition coefficient, molecular

weight, melting point, boiling point and density) are evaluated either singly or in combination to predict human acute toxicity. Acute toxicity in humans is expressed both as oral lethal doses (HLD) and as lethal concentrations (HLC) derived from clinical cases. A comparison has also been made between the individual tests and the conventional rodent tests, as well as between rodent tests and the batteries resulting from partial least squares (PLS), with regard to their predictive power for acute toxicity in humans. Results from univariate regression show that the predictive potential of bioassays (both ecotoxicological and rodent tests) is generally superior to that of individual physicochemical properties for HLD. For HLC prediction, however, no consistent trend could be discerned that indicated whether bioassays are better estimators than physicochemical parameters. Generally, the batteries resulting from PLS regression seem to be more predictive than rodent tests or any of the individual tests. Prediction of HLD appears to be dependent on the phylogeny of the test species: cructaceans, for example, appear to be more important components in the test battery than rotifers and bacteria. For HLC prediction, one anostracan and one cladoceran crustacean are considered to be important. When considering both ecotoxicological tests and physicochemical properties, the battery based on the molecular weight and the cladoceran crustacean predicts HLC substantially better than any other combination.

L55 ANSWER 6 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 89128881 EMBASE
DN 1989128881
TI Effects of drugs and fatty acids related to Reye syndrome on brain **water** content in rats.
AU Katafuchi Y.; Yoshida I.; Yamashita F.; Sinniah D.
CS Department of Pediatrics and Child Health, Kurume University School of Medicine, Kurume 830, Japan
SO Acta Paediatrica Japonica (Overseas Edition), (1989) 31/2 (115-119). ISSN: 0374-5600 CODEN: APDJBE
CY Japan
DT Journal; Journal
FS 030 Pharmacology
037 Drug Literature Index
LA English

L55 ANSWER 7 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 86170011 EMBASE
DN 1986170011
TI Dosage recommendations for activated charcoal-**sorbitol** treatment.
AU Minocha A.; Krenzelok E.P.; Spyker D.A.
CS Department of Internal Medicine, University of Virginia Medical Center, Charlottesville, VA 22908, United States
SO Journal of Toxicology - Clinical Toxicology, (1985) 23/7-8 (579-587). CODEN: JTCTDW
CY United States
DT Journal
FS 037 Drug Literature Index
052 Toxicology
030 Pharmacology
LA English
AB Activated charcoal-**sorbitol** mixture is used for the treatment of

acute poisoning. Based on our experience with healthy adults, overdosed patients and published reports, we have devised a protocol for use of this mixture in different concentrations of **sorbitol**. The dose is based on the size of the patient, type of poison, and the clinical status.

In seriously ill adult patients, we recommend the use of 1 g/kg of activated charcoal in 4.3 ml/kg body weight of 70% **sorbitol** every 4 hours until the first stool containing charcoal appears. In children and ambulatory adults, the same dose of activated charcoal may be administered in 4.3 ml/kg body weight of 35% **sorbitol**. Patients requiring multple doses may be administered activated charcoal as **aqueous** and **sorbitol** suspensions alternately every 2-6 hours after the first charcoal stool has appeared. The patients on multiple dose regimen, especially children, should be closely monitored for any fluid or electrolyte imbalance or depletion of essential vitamins.

L55 ANSWER 8 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 86092149 EMBASE
DN 1986092149
TI Effects of **acetaminophen** on cadmium metabolism in mice.
AU Gale G.R.; Atkins L.M.; Smith A.B.; et al.
CS Veterans Administration Medical Center, Charleston, SC 29403, United States
SO Toxicology and Applied Pharmacology, (1986) 82/2 (368-377).
CODEN: TXAPA
CY United States
DT Journal
FS 037 Drug Literature Index
030 Pharmacology
052 Toxicology
023 Nuclear Medicine
048 Gastroenterology
LA English
AB **Acetaminophen** (ACM) administration to mice of the (C57BL/6 x DBA/2)F1 strain produced a typical hepatic centrilobular necrosis similar to that observed in rodents and humans. To determine the effects of this drug-induced necrosis on cadmium (Cd) metabolism, mice were given a sublethal dose of CdCl2 .cntdot. 2.5 **H2O** containing 109CdCl2 and maintained for a period of time sufficient for Cd-metallothionein (Cd-MT) to be synthesized and distributed. Subsequent administration of ACM ip or po evoked a marked redistribution of Cd from livers to kidneys of mice, and increased the amount of Cd excreted in urine and feces. There were only minimal or no effects on Cd concentrations in other organs assessed. The effect of ACM on Cd redistribution was antagonized by administration of cysteine, a glutathione precursor, and was enhanced by pretreatment with **phenobarbital**, a potent inducer of the cytochrome P-450 mixed-function-oxidase system. Preteatment of mice with ACM 6 or 24 hr prior to Cd administration caused aberrations of the normal Cd distribution pattern, but no effect was noted when Cd administration was delayed for 48 hr after ACM injection, indicating recovery of the mechanisms of Cd-MT synthesis and sequestration. Sephadex G-75 gel filtration chromatography of serum from ACM-treated mice showed that most of the Cd was associated with high-molecular-weight proteins, and only a minor portion was present as Cd-MT. Cd excreted in urine was predominantly in a low-molecular-weight form, but there was evidence of two minor

components of higher molecular weight, neither of which eluted as Cd-MT. Cd excreted in feces was insoluble following homogenization in 0.25 M **sucrose** solution. Cd in livers and kidneys of ACM-treated mice eluted as Cd-MT. It was concluded that persons who have a moderately high Cd burden may be at risk of Cd nephrotoxicity if they incur hepatic necrosis subsequent to ACM abuse.

L55 ANSWER 9 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 85225805 EMBASE
DN 1985225805
TI Effects of **phenobarbital**, phorone and carbon tetrachloride pretreatment on the biliary excretion of **acetaminophen** in rats.
AU Loeser W.; Siegers C.-P.
CS Institut fur Toxikologie der Medizinischen Hochschule Lubeck, D-2400 Lubeck, Germany
SO Archives Internationales de Pharmacodynamie et de Therapie, (1985) 275/2 (180-188).
CODEN: AIPTAK
CY Belgium
DT Journal
FS 037 Drug Literature Index
052 Toxicology
LA English
AB Rats with cannulated bile ducts excreted 24.6% of an i.v. dose of 100 mg/kg **acetaminophen** (AA) into bile within 8 hr, 0.9% as unchanged drug, 5.5% as sulfate, 15.1% as **glucuronide** and 3.1% as the glutathione conjugate. Pretreatment with **phenobarbital** (0.1% solution for 7 days instead of drinking **water**) significantly decreased the amount of total AA recovered in bile, to 12.8%
mainly as a consequence of reduced **glucuronide** excretion (3.5%), whereas the GSH-conjugate was augmented to 6.3%. Pretreatment with the GSH-depletor phorone (250 mg/kg i.p. 1 hr prior to AA) slightly reduced the total recovery of AA to 19.2%, due to a diminished excretion of the **glucuronide** (10.3%). Liver damage due to carbon tetrachloride administration (0.5 ml/kg p.o. 24 hr prior to AA) markedly decreased the total recovery of AA to 8.9% as a consequence of the reduction of the **glucuronic** acid (5.0%) and the GSH-conjugates (0.2%). These observations are discussed with respect to the effects of **phenobarbital**, phorone and CCl4 on microsomal and cytosolic GSH-dependent enzymes involved in the metabolism of AA.

L55 ANSWER 10 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 83167190 EMBASE
DN 1983167190
TI Reactive metabolites of phenacetin and **acetaminophen**: A review.
AU Hinson J.A.
CS Natl. Cent. Toxicol. Res., Jefferson, AR 72079, United States
SO Environmental Health Perspectives, (1983) Vol. 49/- (71-79).
CODEN: EVHPAZ
CY United States
DT Journal
FS 037 Drug Literature Index
030 Pharmacology
031 Arthritis and Rheumatism
035 Occupational Health and Industrial Medicine
052 Toxicology
LA English
AB Phenacetin can be metabolized to reactive metabolites by a variety of

mechanisms. (1) Phenacetin can be N-hydroxylated, and the resulting N-hydroxyphenacetin can be sulfated or **glucuronidated**. Whereas phenacetin N-O sulfate imediately rearranges to form a reactive metabolite which may covalently bind to protein, phenacetin N-O flucuronide slowly rearranges to form reactive metabolites. Incubation of the purified phenacetin N-O **glucuronide** under a variety of conditions suggests that N-acetyl-p-benzoquinone imine is a reactive metabolite. This metabolite covalently binds to protein, reacts with glutathione to form an **acetaminophen**-glutathione conjugate, is reduced by ascorbate to **acetaminophen** or is partially hydrolyzed to acetamide, (2) Phenacetin can be O-deethylated to **acetaminophen**, and **acetaminophen** can be converted directly to a reactive metabolite which may be also N-acetyl-p-benzoquinone imine. (3) Phenacetin can be sequentially N- hydroxylated and O-deethylated to N-hydroxyacetaminophen which spontaneously dehydrates to N-acetyl-p-benzoquinone imine. (4) Phenacetin can be 3,4-epoxidated to form an alkylating and an arylating metabolite. In the presence of glutathione, a S-ethylglutathione conjugate and an **acetaminophen**-glutathione conjugate are formed. In the absence of glutathione, the alkylating metabolite may bind to protein and the arylating metabolite is completely hydrolyzed to acetamide and another arylating metabolite which may bind to protein. The structures of the alkylating and arylating metabolites are unknown. Control experiments have shown that in pathway (1) the phenolic oxygen of the **acetaminophen** -glutathione conjugate is derived from **water**, whereas in pathways (2) and (3) the phenolic oxygen of this metabolite is derived from phenacetin. In pathway (4) the phenolic oxygen was 50% derived from molecular oxygen and 50% from phenacetin. Administration of [p-18O]phenacetin to hamsters revealed only a 10% loss of 18O in the **acetaminophen** mercapturic acid (the further metabolic product of the glutathione conjugate) which suggests that, in the hamster, pathways (2) and/or (3) are the primary mechanism of conversion of phenacetin to reactive metabolites in vivo.

L55 ANSWER 11 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 83103551 EMBASE
DN 1983103551
TI Drug induced changes in **water** excretion.
AU Gardenswartz M.H.; Berl T.
CS Dep. Med., Univ. Colorado Health Sci. Cent., Denver, CO 80262, United States
SO Kidney, (1981) 14/1 (19-23).
CODEN: KIDNAI
CY United States
DT Journal
FS 038 Adverse Reactions Titles
037 Drug Literature Index
028 Urology and Nephrology
018 Cardiovascular Diseases and Cardiovascular Surgery
003 Endocrinology
006 Internal Medicine
007 Pediatrics and Pediatric Surgery
LA English

L55 ANSWER 12 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 82174099 EMBASE
DN 1982174099
TI [Intoxication by **water** and antidiuresis conditions].
LES INTOXICATIONS PAR L'EAU ET LES ETATS D'ANTIDIURESE.
AU Rince M.; Charmes J.P.; Leroux-Robert C.
CS Serv. Nephrol., CHU Dupuytren, 87000 Limoges, France
SO Revue du Praticien, (1982) 32/21 (1427-1439).
CODEN: REPRA3
CY France
DT Journal
FS 038 Adverse Reactions Titles
037 Drug Literature Index
003 Endocrinology
028 Urology and Nephrology
LA French
SL English

L55 ANSWER 13 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 81176411 EMBASE
DN 1981176411
TI Hyponatremia.
AU Goldberg M.
CS Dept. Int. Med., Univ. Cincinnati Coll. Med., Cincinnati, Ohio, United States
SO Medical Clinics of North America, (1981) 65/2 (251-269).
CODEN: MCNAA
CY United States
DT Journal
FS 006 Internal Medicine
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
029 Clinical Biochemistry
002 Physiology
LA English
AB It is now abundantly clear that regulation of the plasma (or serum) sodium concentration (P(Na)) is the major determinant of the osmotic forces in the extracellular fluid. Since mammalian cell membranes are freely permeable to **water**, this means that all body fluids are in osmotic equilibrium and that changes in P(Na) may be associated with rapid and major shifts of **water** into and out of the cells. This has special implications regarding the clinical manifestations of hyponatremia in the central nervous system, since brain cell expansion in hyponatremic states is limited by the confines of the cranial vault. Fortunately the body has a well developed system of homeostatic osmoregulatory mechanisms oriented toward the regulation of the P(Na) and therefore the plasma osmolality (Posm) within a narrow range (i.e., between 285 and 299 mOsm/kg **H2O**). These mechanisms will be summarized briefly before undertaking a more detailed review of the clinical hyponatremic states, their differential diagnosis and management.

L55 ANSWER 14 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 81110922 EMBASE
DN 1981110922
TI Specific modalities of therapy for inappropriate antidiuretic hormone

secretion.
AU Sordillo P.; Matarese R.A.; Novich R.K.; et al.
CS Nephrol. Sect., Dept. Med., Lenox Hill Hosp., New York, N.Y. 10021, United States
SO Clinical Nephrology, (1981) 15/3 (107-110).
CODEN: CLNHBI
CY Germany
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
LA English
AB In addition to general therapeutic maneuvers which will correct hypoosmolality in all patients with SIADH, there also exist precise remedies which can successfully treat SIADH in a specific manner. When the diagnosis of SIADH is made, general measures such as **water** restriction and salt replacement should be started, and more vigorous therapeutic maneuvers such as the use of concentrated salt solutions and diuretics should be considered. In addition, however, consideration must also be given to the specific type of SIADH that is to be treated. As illustrated, if endogenous excessive ADH secretion has resulted either from a drug which stimulates ADH release, or from stimuli arising elsewhere in the organism such as may occur with extensive pulmonary or central nervous system disease, use of an agent which can suppress ADH secretion, such as phenytoin, in usual doses, should be considered. Furthermore, if SIADH secondary to neoplasm is encountered, the use of demeclocycline, an agent which blocks ADH effect at the level of the collecting tubule, will prove most efficacious. This agent may be used in low doses for extended periods of time if necessary, if careful follow-up for evidence of renal, or other, toxicity is made. Finally, the diagnosis of **glucocorticoid** deficiency should always be considered when SIADH is encountered since this disorder can be rapidly corrected by **glucocorticoid** administration. In addition, this diagnosis may also alert the physician to the possibility of other serious hormone deficiencies.

L55 ANSWER 15 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 80226167 EMBASE
DN 1980226167
TI [Rehydration per os in the treatment of children suffering from measles in Africa].
LA REHYDRATATION PAR VOIE ORALE. SON UTILISATION AU COURS DU TRAITEMENT D'ENFANTS ROUGEOLEUX.
AU Samba-Lefebvre M.C.
CS Serv. Maladies Infect. Makelekele, Brazzaville, Congo
SO Lyon Medical, (1980) 243/11 (655-660).
CODEN: LYMEAN
CY France
DT Journal
FS 037 Drug Literature Index
007 Pediatrics and Pediatric Surgery
047 Virology
LA French
SL English
AB This paper is a report concerning the use of rehydration per os in the treatment of measles. In Africa the formula of the solution used was as follows: (for 1 litre of **water**) **glucose**: 20 g;

NaCl:3.5g;KCl:1.5g; NaHCO3: 2.5 g. The solution was administered when there was a risk of dehydration or when a state of dehydration already existed. In order to assess its effectiveness, a comparison was made over two consecutive periods during which 250 patients were hospitalized, of the number of patients undergoing intravenous perfusion and the total quantity of fluid perfused; rehydration per os was used during the second of the two periods, not during the first. The salt-**glucose** solution reduced by 64% the number of patients undergoing intravenous perfusion, and by 75% the total anount of fluid perfused. This resulted in a total economy of 64% in the cost of treatment during the second period. Rehydration per os is a simple, non-traumatic, economic and above all effective method. It should restrict the use of parenteral rehydration to a very small number of patients.

L55 ANSWER 16 OF 19 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 75010671 EMBASE
DN 1975010671
TI Tuberculosis of central nervous system. Part II: Clinical aspects.
AU Udani P.M.; Bhat U.S.
CS Inst. Child Hlth, J.J. Group Hosp., Grant Med. Coll., Bombay, India
SO Indian Pediatrics, (1974) 11/1 (7-17).
CODEN: INPDAR
DT Journal
FS 037 Drug Literature Index
007 Pediatrics and Pediatric Surgery
LA English
AB This survey of the clinical aspects of tuberculosis cerebrospinalis in children covers the typical picture at onset, and the several types of its course. Diagnostic clues are presented and a treatment scheme is proposed.
The recovery rate in this study depended on the socioeconomic group, ranging from 85% in upper class people to 25% in the economically poor group. (42 references.)

L55 ANSWER 17 OF 19 DRUGB COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 73-31947 DRUGB T S E
TI STEVENS-JOHNSON SYNDROME ASSOCIATED WITH DIPHENYL-HYDANTOIN THERAPY. A CASE REPORT.
AU BOSSO J A JR.; CHUDZIK G M
LO BUFFALO,N.Y.,USA.
SO DRUG INTEL.CLIN.PHARM. (7, NO.8, 336-339, 1973)
DT Journal

L55 ANSWER 18 OF 19 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 98-437043 [37] WPIDS
DNC C98-132804
TI New burst-free, sustained, programmable release composition(s) - containing an active material in a blend of uncapped and end-capped co polymer, preferably a poly (DL-lactide-co glycolide).
DC A96 B04 B05 B07 D16
IN BOEDEKER, E C; FRIDEN, P; JACOB, E; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; TICE, T R; VAN HAMONT, J E
PA (USSA) US SEC OF ARMY
CYC 79
PI WO 9832427 A1 980730 (9837)* EN 422 pp
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9863175 A 980818 (9851)

ADT WO 9832427 A1 WO 98-US1556 980127; AU 9863175 A AU 98-63175 980127

FDT AU 9863175 A Based on WO 9832427

PRAI US 97-789734 970127

AN 98-437043 [37] WPIDS

AB WO 9832427 A UPAB: 980916

A composition is claimed for the burst-free, sustained, programmable release of active material(s) over a period from 1-100 days, comprising: (a) an active material; and (b) a carrier which may contain pharmaceutically-acceptable adjuvant, comprised of a blend of uncapped and end-capped biodegradable-biocompatible copolymer.

Also claimed are: (1) a process for preparing controlled release compositions characterised by burst-free, sustained, programmable release of biologically active agents, comprising: (a) dissolving biodegradable poly(lactide/glycolide), in uncapped or end-capped form in methylene chloride, and dissolving a biologically active agent or active core in **water**; (b) adding the **aqueous** layer to the polymer solution and emulsifying to provide an inner **water**-in-oil (w/o) emulsion; (c) stabilising the w/o emulsion in a solvent-saturated **aqueous** phase containing a oil-in-**water** (o/w) emulsifier; (d) adding the w/o emulsion to an external **aqueous** layer containing o/w emulsifier to form a ternary emulsion; and (e) stirring the resulting **water**-in-oil-in-**water** (w/o/w) emulsion to remove the solvent, and rinsing hardened microcapsules with **water** and lyophilising the hardened microcapsules; (2) a method for the protection against infection of a mammal by pathogenic organisms comprising administering orally to the mammal an immunogenic amount of an immunostimulating composition consisting of an antigenic synthetic peptide encapsulated within a poly(lactide/galactide) matrix; (3) a vaccine for the immunisation of a mammal against infection by pathogenic organisms consisting of an antigen in an amount of 0.1-1% encapsulated within a biodegradable-biocompatible polymeric poly(DL-lactide-co-glycolide) matrix where the polymer is end-capped or a blend of uncapped and end-capped polymers; and (4) an immunostimulating composition comprising encapsulating-microspheres, which may contain an adjuvant, where the microspheres having a diameter of 1 nm to 10 microns are comprised of: (a) a biodegradable-biocompatible poly (DL-lactide-co-glycolide) as the bulk matrix, where the copolymer (lactide to glycolide L/G) ratio for uncapped and end-capped polymer is 0/100 to 1/99; and (b) an immunogenic substance comprising a bacteria, virus, fungus, parasite, or derivative, that serves to elicit the production of antibodies in animal subjects.

USE - The biocompatible and biodegradable microspheres can provide programmable sustained release of biologically active agents, including polypeptides over a period of up to 100 days in an **aqueous** physiological environment with little or no burst release. They can be used for the delivery of e.g. insulins, AZT, diethyl silbestrol, 17-beta-oestradiol, oestron, ethinyl estradiol, mestranol, norethindrone, norgestryl, ethynodiol diacetate, lynoestrenol, medroxyprogesterone acetate, dimethisterone, megestrol acetate, chlormadinine acetate, norgestimate, norethisterone, ethisterone, melentate, norgestimate,

norethisterone, ethisterone, melentate, melengestrol, norethynodrel, nonylphenoxypolyoxyethylene **glycol**, benzethonium chloride, chlorindanol, aluminium hydroxide, calcium carbonate, magnesium carbonate, sodium carbonate, chloropromaquine HCl, clozapine, mesoridazine, metiapine, reserpine, thioridazine, chlordiazepoxide, diazepam, meprobamate, temazepam, codeine, **phenobarbital**, sodium pentobarbital, sodium secobarbital, testosterone, testosterone propionate, sulphonamides, 4-aminoquinolines, 8-aminoquinolines, pyrimethamine, mazindol. phentermine, L-dopa, atropine, methscopolamine bromide, dextromethorphan, noscapine, Rauwolfia alkaloids, nitroglycerin, organic nitrites, pentaerythriotetranitrate, potassium chloride, ergotamine with and without caffeine, hydrogenated ergot alkaloids, dihydroergocristine methanesulphate, dihydrooergocornine methanesulphonate, dihydroergokroyptine methanesulphate, atropine sulphate, Belladonna, hyoscine hydrobromide, dihydrocodienone, meperidine, morphine, salicylates, asprin, **acetaminophen**, d-propoxyphene, ceflacor, cefuroxime, chloramphenical, gentamycin, Kanamycin A, Kanamycin B, ampicillin, amoxicillin, streptomycin A, antimycin A, chloropamtheniol, metromidazole, oxytetracycline, penicillin G, minocycline, ciprofloxacin, ofoxacin, clarithromycin, frythromycin (sic), gentamicin, amikacin, tobramycin, kanamycin, ampicillin, polymyxin-B, amphotericin-B, aztrofonam, chloramphenicol, fusidans, lincosamides, metronidazole, nitro-furantion, imipenem/cilastin, quinolones, rifampin, polyenes, sulphonamides, trimethoprim, vancomycin, teicoplanin, imidazoles, mephenytoin, **phenobarbital**, trimethadione, triethylperazine, chlorophinazine, dimenhydrinate, diphenhydramine, perphenazine, tripelennamine, hydrocortisone, prednisolone, prednisone, allopurinol, indomethacin, phenylbutazone, prostaglandin, thiotepa, chloramucil, cyclophosphamide, melphalan, nitrogen mustard, methotrexate, aztreonam, and refampin.

Dwg.0/54

L55 ANSWER 19 OF 19 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 91-239882 [33] WPIDS
DNC C91-104244
TI Syrup compsn. contg. **acetaminophen** or **phenobarbital** - contains poly hydric alcohol and/or polymer of poly hydric alcohol and **water**-soluble macromolecule.
DC A96 B03 B05
IN KAWASAKI, Y; SUZUKI, Y
PA (KAWA-I) KAWASAKI Y; (SHOY) SHOWA YAKUHIN KAKO KK
CYC 6
PI EP 441307 A 910814 (9133)* 11 pp
R: DE FR GB
CA 2035693 A 910807 (9142)
JP 03232816 A 911016 (9148)
US 5154926 A 921013 (9244) 5 pp
EP 441307 B1 940921 (9436) EN 10 pp
R: DE FR GB
DE 69104079 E 941027 (9442)
JP 07014872 B2 950222 (9512) 4 pp
CA 2035693 C 970204 (9717)
EP 441307 B2 980408 (9818) EN 10 pp
R: DE FR GB
ADT EP 441307 A EP 91-101494 910205; JP 03232816 A JP 90-26943 900206; US 5154926 A US 91-651298 910206; EP 441307 B1 EP 91-101494 910205; DE 69104079 E DE 91-604079 910205, EP 91-101494 910205; JP 07014872 B2 JP

90-26943 900206; CA 2035693 C CA 91-2035693 910205; EP 441307 B2 EP 91-101494 910205
FDT DE 69104079 E Based on EP 441307; JP 07014872 B2 Based on JP 03232816
PRAI JP 90-26943 900206
AN 91-239882 [33] WPIDS
AB EP 441307 A UPAB: 930928
A syrup compsn. comprises **acetaminophen** (I) or **phenobarbital** (II), a **polyhydric** alcohol and/or its polymer, and a **water**-soluble macromolecule, in wt. ratios (I):polyol/polymer 1:1-1:10 and (I): macromolecule 1:0.1-1:2 or (II):polyol/polymer 1:20-1:100 and (II):macromolecule 1:1-1:20.

The polygol is ethylene **glycol**, propylene **glycol** or **glycerol**, and its polymer is polyethylene **glycol** or polypropylene **glycol**. Esp. the polyol/polymer is a mixt. of 1-30 wt.% propylene **glycol**, greater than 20 wt.% PEG and greater than 5 wt.% **glycerol**. The **water**-soluble macromolecule is polyvinyl pyrrolidone, gum arabic, gelatin or polyvinyl polypyrrolidone. The wt. ratio of (I):polyol/polymer is 1:3-1:7 and wt. ratio (I):macromolecule is 1:0.1-1:1.25. The wt. ratio of (II):polyol/polymer is 1:40-1:60 and wt.ratio (II):macromolecule is 1:1-1:10.

USE/ADVANTAGE - (I) is useful in treatment of fever and pain, and (II) is useful in treatment of insomnia, nervous excitement, convulsion, autonomic seizure and psychomotor seizure. The bitter taste of (I) or (II) is effectively masked. The syrup can provide therapeutic effects at low doses, and is useful for paediatric admin. since it is easy to take. 0/0

ABEQ US 5154926 A UPAB: 930928
Aq. oral pharmaceutical compsns. in syrup form comprise (a) **acetaminophen** in an amt. of 1-4g in 100 ml of compsn.; (b) a **polyhydric** alcohol and/or **polyhydric** alcohol polymer of mol. wt. 300-400 and (c) polyvinyl pyrrolidone, gum arabic powder, gelatin or polyvinyl polypyrrolidone. The wt. ratio (a):(b) is 1:1 to 1:10 and the wt. ratio (a):(b) is 1:0-1:2.

The **polyhydric** alcohol is pref. ethylene **glycol**, propylene **glycol** and **glycerol** and the **polyhydric** alcohol polymer is pref. polyethylene **glycol** or polypropylene **glycol**. Similar compsns. contg. 0.2-0.5 g/100 ml of **phenobarbital** instead of **acetaminophen** are also claimed.

ADVANTAGE - The compsns. have reduced bitter taste. 0/0

ABEQ EP 441307 B UPAB: 980507
A syrup compsn. comprises **acetaminophen** (I) or **phenobarbital** (II), a **polyhydric** alcohol and/or its polymer, and a **water**-soluble macromolecule, in wt. ratios (I):polyol/polymer 1:1-1:10 and (I): macromolecule 1:0.1-1:2 or (II):polyol/polymer 1:20-1:100 and (II):macromolecule 1:1-1:20.

The polygol is ethylene **glycol**, propylene **glycol** or **glycerol**, and its polymer is polyethylene **glycol** or polypropylene **glycol**. Esp. the polyol/polymer is a mixt. of 1-30 wt.% propylene **glycol**, greater than 20 wt.% PEG and greater than 5 wt.% **glycerol**. The **water**-soluble macromolecule is polyvinyl pyrrolidone, gum arabic, gelatin or polyvinyl polypyrrolidone. The wt. ratio of (I):polyol/polymer is 1:3-1:7 and wt. ratio (I):macromolecule is 1:0.1-1:1.25. The wt. ratio of (II):polyol/polymer is

1:40-1:60 and wt.ratio (II):macromolecule is 1:1-1:10.

USE/ADVANTAGE - (I) is useful in treatment of fever and pain, and (II) is useful in treatment of insomnia, nervous excitement, convulsion, autonomic seizure and psychomotor seizure. The bitter taste of (I) or (II) is effectively masked. The syrup can provide therapeutic effects at low doses, and is useful for paediatric admin. since it is easy to take. Dwg.0/0

=> d bib abs l60 1-12

L60 ANSWER 1 OF 12 MEDLINE
AN 96098190 MEDLINE
DN 96098190
TI Drug release from new bioartificial hydrogel.
AU Gayet J C; Fortier G
CS Departement de chimie-biochimie, Universite du Quebec `a Montreal, Canada.
SO ARTIFICIAL CELLS, BLOOD SUBSTITUTES, AND IMMOBILIZATION BIOTECHNOLOGY, (1995) 23 (5) 605-11.
Journal code: BXE. ISSN: 1073-1199.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199604
AB The use of high **water** content (> 96%) hydrogels obtained from copolymerisation of bovine serum albumin and poly(ethylene **glycol**) as a controlled release system has been investigated. Such hydrogels allowed release of soluble and hydrophobic substances, even proteins. Release is shown to occur by a diffusion controlled mechanism, leading to half-life times of release ranging between 0.8 hour for theophylline and 4.2 hours for lysozyme, when a 2.4 mm thick disc of BSA-PEG (MW of 10000) was used. The effect of the porosity of the hydrogel on the diffusive properties of theophylline and **hydrocortisone** has been evaluated by varying the molecular weight of the poly(ethylene **glycol**). It was shown that poly(ethylene **glycol**) of high molecular weight leads to more porous hydrogels in which the diffusion is faster.

L60 ANSWER 2 OF 12 MEDLINE
AN 92318140 MEDLINE
DN 92318140
TI Influence of D-**glucose**-induced **water** absorption on rat jejunal uptake of two passively absorbed drugs.
AU Lu H H; Thomas J; Fleisher D
CS College of Pharmacy, University of Michigan, Ann Arbor 48109-1065..
NC 1 R29 NS24616-03 (NINDS)
SO JOURNAL OF PHARMACEUTICAL SCIENCES, (1992 Jan) 81 (1) 21-5.
Journal code: JO7. ISSN: 0022-3549.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
AB The intestinal absorption of D-**glucose** is coupled to transepithelial sodium transport and this process generates intestinal **water** absorption. In situ jejunal perfusions were performed in rats to determine the extent of **water** transport as a function of perfusion flow rate, perfusate osmolality, and D-**glucose** concentration. Jejunal perfusions of iso-osmolar D-**glucose**, at flow rates and concentrations representative of the fed state, increased the dimensionless membrane permeabilities of the analgesic **acetaminophen** from 0.6 to 1.4, and that of the **corticosteroid** prednisolone from 1.6 to 2.2. This increase is less important for the more hydrophobic prednisolone since its baseline permeability (1.6) is indicative of complete uptake from solution, while the lower baseline permeability (0.6) of the more hydrophilic

acetaminophen represents incomplete membrane uptake. The results suggest that nutrient-induced **water** transport can enhance jejunal uptake of small hydrophilic solutes. This phenomenon may contribute to variability in the absorption of drugs in this physicochemical class during the fed state.

L60 ANSWER 3 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1992:122771 BIOSIS
DN BA93:68571
TI INFLUENCE OF D **GLUCOSE**-INDUCED **WATER** ABSORPTION ON RAT JEJUNAL UPTAKE OF TWO PASSIVELY ABSORBED DRUGS.
AU LU H-H; THOMAS J; FLEISHER D
CS COLLEGE PHARMACY, UNIV. MICHIGAN, ANN ARBOR, MICH. 48109-1065.
SO J PHARM SCI, (1992) 81 (1), 21-25.
CODEN: JPMSAE. ISSN: 0022-3549.
FS BA; OLD
LA English
AB The intestinal absorption of D-**glucose** is coupled to transepithelial sodium transport and this process generates intestinal **water** absorption. In situ jejunal perfusions were performed in rats to determine the extent of **water** transport as a function of perfusion flow rate, perfusate osmolality, and D-**glucose** concentrations. Jejunal perfusion of isoosmolar D-**glucose**, at flow rates and concentrations representative of the fed state, increased the dimensions membrane permeabilities of the analgesic acetaminopen from 0.6 to 1.4, and that of the **corticosteroid** prednisolone from 1.6 to 2.2. This increase is less important for the more hydrophobic prednisolone since its baseline permeability (1.6) is indicative of complete uptake from solution, while the lower baseline permeability (0.6) of the more hydrophilic **acetaminophen** represents incomplete membrane uptake. The results suggest that nutrient-induced **water** transport can enhance jejunal uptake of small hydrophilic solutes. This phenomenon may contribute to variability in the absorption of drugs in this physicochemical class during the fed state.

L60 ANSWER 4 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1998279829 EMBASE
TI The hydrophobic effect. 1. A consequence of the mobile order in H- bonded liquids.
AU Ruelle P.; Kesselring U.W.
CS P. Ruelle, Institut d'Analyse Pharmaceutique, Section de Pharmacie, Universite de Lausanne, CH-1015 Lausanne, Switzerland. Paul.Ruelle@iap.unil.ch
SO Journal of Pharmaceutical Sciences, (1998) 87/8 (987-997).
Refs: 121
ISSN: 0022-3549 CODEN: JPMSAE
CY United States
DT Journal; Article
FS 037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB The hydrophobic effect has an entropic nature that cannot be explained by classical multicomponent treatments that do not explicitly take into account both the mobility and the nonergodicity of the H-bonds in amphiphilic liquids. The nonergodic thermodynamics of mobile order in H-bonded liquids based on time fractions rather than on concentrations

provides a novel qualitative and quantitative explanation for the molecular origin of the hydrophobic effect. Chiefly, this effect corresponds to the loss of the mobile order entropy of associated molecules by dilution with foreign substances. Not being a unique property of **water**, the propensity of an amphiphilic solvent to induce a solvophobic effect increases primarily as its structuration factor increases, and secondarity as the solute/solvent molar volume ratio increases. On this basis, it can be expected that in the absence of strong solute-solvent specific interactions, the solubility of nonelectrolytes will generally decrease in the following order: butanol > propanol > ethanol > methanol > propylene **glycol** > ethylene **glycol** > formamide > **water**.

L60 ANSWER 5 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96094831 EMBASE
DN 1996094831
TI High **water** content BSA-PEG hydrogel for controlled release device: Evaluation of the drug release properties.
AU Gayet J.-C.; Fortier G.
CS Laboratoire d'Enzymologie Appliquee, Departement de Chimie-Biochimie, Universite du Quebec a Montreal, C.P. 8888, Succ. Centre-Ville,Montreal, Que. H3C 3P8, Canada
SO Journal of Controlled Release, (1996) 38/2-3 (177-184).
ISSN: 0168-3659 CODEN: JCREEC
CY Netherlands
DT Journal; Article
FS 027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The use as a controlled release system of high **water** content (>96%) hydrogels, obtained from the copolymerization of bovine serum albumin and poly(ethylene **glycol**), has been investigated. Such hydrogels allowed the release of hydrophilic and hydrophobic substances, and even of small proteins. It was demonstrated using seven different drugs and one protein that the mechanism of release by the hydrogel matrix was a Fickian diffusion-controlled process. The half-lives of release for theophylline and lysozyme were 0.8 and 4.2 h, respectively. The effect of the porosity of the hydrogel on the diffusive properties of theophylline and **hydrocortisone** was evaluated by varying the molecular mass of the poly(ethylene **glycol**) and the OH/NH2 molar ratio used for the synthesis of the hydrogel. High molecular masses of poly(ethylene **glycol**) and low OH/NH2 molar ratios of reagents led to hydrogels becoming more porous, allowing faster rates of diffusion. The control of diffusion was also studied by tailoring the thickness of the hydrogel. For theophylline, an increase in the half-life of release from 0.26 to 1.98 h was observed when the thickness of the slab was increased from 0.1 to 0.3 cm. Also, as expected, the rate of diffusion was independent of the concentration of the drug in the hydrogel. We believe that this family of BSA-PEG hydrogels could be useful for the preparation of controlled release devices in the field of wound dressing.

L60 ANSWER 6 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 92074018 EMBASE

DN 1992074018
TI Influence of D-**glucose**-induced **water** absorption on rat jejunal uptake of two passively absorbed drugs.
AU Lu H.-H.; Thomas J.; Fleisher D.
CS College of Pharmacy, University of Michigan, Ann Arbor, MI 48109-1065, United States
SO Journal of Pharmaceutical Sciences, (1992) 81/1 (21-25). ISSN: 0022-3549 CODEN: JPMSAE
CY United States
DT Journal; Article
FS 048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The intestinal absorption of D-**glucose** is coupled to transepithelial sodium transport and this process generates intestinal **water** absorption. In situ jejunal perfusions were performed in rats to determine the extent of **water** transport as a function of perfusion flow rate, perfusate osmolality, and D-**glucose** concentration. Jejunal perfusions of isoosmolar D-**glucose**, at flow rates and concentrations representative of the fed state, increased the dimensionless membrane permeabilities of the analgesic **acetaminophen** from 0.6 to 1.4, and that of the **corticosteroid** prednisolone from 1.6 to 2.2. This increase is less important for the more hydrophobic prednisolone since its baseline permeability (1.6) is indicative of complete uptake from solution, while the lower baseline permeability (0.6) of the more hydrophilic **acetaminophen** represents incomplete membrane uptake. The results suggest that nutrient-induced **water** transport can enhance jejunal uptake of small hydrophilic solutes. This phenomenon may contribute to variability in the absorption of drugs in this physicochemical class during the fed state.

L60 ANSWER 7 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 85022551 EMBASE
DN 1985022551
TI Solid state reactions. Theoretical and experimental aspects.
AU Monkhouse D.C.; Van Campen L.
CS Pharmaceutical Research, Squibb Institute for Medical Research, New Brunswick, NJ 08903, United States
SO Drug Development and Industrial Pharmacy, (1984) 10/8-9 (1175-1276). CODEN: DDIPD8
CY United States
DT Journal
FS 037 Drug Literature Index
030 Pharmacology
LA English
AB Implicit in the successful design of a solid dosage form is the assumption that the pharmaceutical scientist has become fully acquainted with the fundamentals of solid state stability. The contents of this article were compiled to give the potential practitioner a grasp of how knowledge of solid state chemistry, experimental methods, and kinetics could facilitate studying factors affecting the stability of solid dosage forms in the broadest sense. Crucial to modern day drug development is the concept that dosage forms introduced to the clinic be commercializable from the

beginning; false starts in a pivotal clinical program can be very costly. Therefore, for stable solid dosage forms to be developed in a rational, intelligent and streamlined fashion, application of the principles described herein is believed to be essential.

L60 ANSWER 8 OF 12 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 75010671 EMBASE
DN 1975010671
TI Tuberculosis of central nervous system. Part II: Clinical aspects.
AU Udani P.M.; Bhat U.S.
CS Inst. Child Hlth, J.J. Group Hosp., Grant Med. Coll., Bombay, India
SO Indian Pediatrics, (1974) 11/1 (7-17).
CODEN: INPDAR
DT Journal
FS 037 Drug Literature Index
007 Pediatrics and Pediatric Surgery
LA English
AB This survey of the clinical aspects of tuberculosis cerebrospinalis in children covers the typical picture at onset, and the several types of its course. Diagnostic clues are presented and a treatment scheme is proposed.
The recovery rate in this study depended on the socioeconomic group, ranging from 85% in upper class people to 25% in the economically poor group. (42 references.)

L60 ANSWER 9 OF 12 DRUGB COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 73-31947 DRUGB T S E
TI STEVENS-JOHNSON SYNDROME ASSOCIATED WITH DIPHENYL-HYDANTOIN THERAPY. A CASE REPORT.
AU BOSSO J A JR.; CHUDZIK G M
LO BUFFALO,N.Y.,USA.
SO DRUG INTEL.CLIN.PHARM. (7, NO.8, 336-339, 1973)
DT Journal

L60 ANSWER 10 OF 12 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 92:35880 SCISEARCH
GA The Genuine Article (R) Number: GY159
TI INFLUENCE OF D-**GLUCOSE**-INDUCED **WATER**-ABSORPTION ON RAT JEJUNAL UPTAKE OF 2 PASSIVELY ABSORBED DRUGS
AU LU H H; THOMAS J; FLEISHER D (Reprint)
CS UNIV MICHIGAN, COLL PHARM, ANN ARBOR, MI, 48109
CYA USA
SO JOURNAL OF PHARMACEUTICAL SCIENCES, (JAN 1992) Vol. 81, No. 1, pp. 21-25.
ISSN: 0022-3549.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 28
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The intestinal absorption of D-**glucose** is coupled to trans-epithelial sodium transport and this process generates intestinal **water** absorption. In situ jejunal perfusions were performed in rats to determine the extent of **water** transport as a function of perfusion flow rate, perfusate osmolality, and D-**glucose** concentration. Jejunal perfusions of iso-osmolar D-**glucose**, at flow rates and concentrations representative of the fed state, increased the dimensionless membrane permeabilities of the analgesic

acetaminophen from 0.6 to 1.4, and that of the **corticosteroid** prednisolone from 1.6 to 2.2. This increase is less important for the more hydrophobic prednisolone since its baseline permeability (1.6) is indicative of complete uptake from solution, while the lower baseline permeability (0.6) of the more hydrophilic **acetaminophen** represents incomplete membrane uptake. The results suggest that nutrient-induced **water** transport can enhance jejunal uptake of small hydrophilic solutes. This phenomenon may contribute to variability in the absorption of drugs in this physicochemical class during the fed state.

L60 ANSWER 11 OF 12 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 98-437043 [37] WPIDS
DNC C98-132804
TI New burst-free, sustained, programmable release composition(s) - containing an active material in a blend of uncapped and end-capped co polymer, preferably a poly (DL-lactide-co glycolide).
DC A96 B04 B05 B07 D16
IN BOEDEKER, E C; FRIDEN, P; JACOB, E; JEYANTHI, R; MCQUEEN, C E; REID, R H; ROBERTS, F D; SETTERSTROM, J A; TICE, T R; VAN HAMONT, J E
PA (USSA) US SEC OF ARMY
CYC 79
PI WO 9832427 A1 980730 (9837)* EN 422 pp
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9863175 A 980818 (9851)
ADT WO 9832427 A1 WO 98-US1556 980127; AU 9863175 A AU 98-63175 980127
FDT AU 9863175 A Based on WO 9832427
PRAI US 97-789734 970127
AN 98-437043 [37] WPIDS
AB WO 9832427 A UPAB: 980916
A composition is claimed for the burst-free, sustained, programmable release of active material(s) over a period from 1-100 days, comprising: (a) an active material; and (b) a carrier which may contain pharmaceutically-acceptable adjuvant, comprised of a blend of uncapped and
end-capped biodegradable-biocompatible copolymer.

Also claimed are: (1) a process for preparing controlled release compositions characterised by burst-free, sustained, programmable release of biologically active agents, comprising: (a) dissolving biodegradable poly(lactide/glycolide), in uncapped or end-capped form in methylene chloride, and dissolving a biologically active agent or active core in **water**; (b) adding the **aqueous** layer to the polymer solution and emulsifying to provide an inner **water**-in-oil (w/o) emulsion; (c) stabilising the w/o emulsion in a solvent-saturated **aqueous** phase containing a oil-in-**water** (o/w) emulsifier; (d) adding the w/o emulsion to an external **aqueous** layer containing o/w emulsifier to form a ternary emulsion; and (e) stirring the resulting **water**-in-oil-in-**water** (w/o/w) emulsion to remove the solvent, and rinsing hardened microcapsules with **water** and lyophilising the hardened microcapsules; (2) a method for the protection against infection of a mammal by pathogenic organisms comprising administering orally to the mammal an immunogenic amount of an immunostimulating composition consisting of an antigenic synthetic peptide

encapsulated within a poly(lactide/galactide) matrix; (3) a vaccine for the immunisation of a mammal against infection by pathogenic organisms consisting of an antigen in an amount of 0.1-1% encapsulated within a biodegradable-biocompatible polymeric poly(DL-lactide-co-glycolide) matrix

where the polymer is end-capped or a blend of uncapped and end-capped polymers; and (4) an immunostimulating composition comprising encapsulating-microspheres, which may contain an adjuvant, where the microspheres having a diameter of 1 nm to 10 microns are comprised of: (a)

a biodegradable-biocompatible poly (DL-lactide-co-glycolide) as the bulk matrix, where the copolymer (lactide to glycolide L/G) ratio for uncapped and end-capped polymer is 0/100 to 1/99; and (b) an immunogenic substance comprising a bacteria, virus, fungus, parasite, or derivative, that serves

to elicit the production of antibodies in animal subjects.

USE - The biocompatible and biodegradable microspheres can provide programmable sustained release of biologically active agents, including polypeptides over a period of up to 100 days in an **aqueous** physiological environment with little or no burst release. They can be used for the delivery of e.g. insulins, AZT, diethyl silbestrol, 17-beta-oestradiol, oestron, ethinyl estradiol, mestranol, norethindrone, norgestryl, ethynodiol diacetate, lynoestrenol, medroxyprogesterone acetate, dimethisterone, megestrol acetate, chlormadinine acetate, norgestimate, norethisterone, ethisterone, melentate, norgestimate, norethisterone, ethisterone, melentate, melengestrol, norethynodrel, nonylphenoxypolyoxyethylene **glycol**, benzethonium chloride, chlorindanol, aluminium hydroxide, calcium carbonate, magnesium carbonate,

sodium carbonate, chloropromaquine HCl, clozapine, mesoridazine, metiapine, reserpine, thioridazine, chlordiazepoxide, diazepam, meprobamate, temazepam, codeine, phenobarbital, sodium pentobarbital, sodium secobarbital, testosterone, testosterone propionate, sulphonamides,

4-aminoquinolines, 8-aminoquinolines, pyrimethamine, mazindol. phentermine, L-dopa, atropine, methscopolamine bromide, dextromethorphan, noscapine, Rauwolfia alkaloids, nitroglycerin, organic nitrites, pentaerythriotetranitrate, potassium chloride, ergotamine with and without

caffeine, hydrogenated ergot alkaloids, dihydroergocristine methanesulphate, dihydrooergocornine methanesulphonate, dihydroergokroyptine methanesulphate, atropine sulphate, Belladonna, hyoscine hydrobromide, dihydrocodienone, meperidine, morphine, salicylates, asprin, **acetaminophen**, d-propoxyphene, ceflacor, cefuroxime, chloramphenical, gentamycin, Kanamycin A, Kanamycin B, ampicillin, amoxicillin, streptomycin A, antimycin A, chloropamtheniol, metromidazole, oxytetracycline, penicillin G, minocycline, ciprofloxacin, ofoxacin, clarithromycin, frythromycin (sic), gentamicin, amikacin, tobramycin, kanamycin, ampicillin, polymyxin-B, amphotericin-B, aztrofonam, chloramphenicol, fusidans, lincosamides, metronidazole, nitro-furantion, imipenem/cilastin, quinolones, rifampin, polyenes, sulphonamides, trimethoprim, vancomycin, teicoplanin, imidazoles, mephenytoin, phenobarbital, trimethadione, triethylperazine, chlorophinazine, dimenhydrinate, diphenhydramine, perphenazine, tripelennamine, **hydrocortisone**, prednisolone, prednisone, allopurinol, indomethacin, phenylbutazone, prostaglandin, thiotepa, chloramucil, cyclophosphamide, melphalan, nitrogen mustard, methotrexate, aztreonam, and refampin.

Dwg.0/54

L60 ANSWER 12 OF 12 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 88-322646 [45] WPIDS
CR 88-322645 [45]; 90-224510 [29]; 90-320018 [42]; 91-086863 [12]; 91-215173 [29]; 93-145785 [18]; 93-167290 [20]; 93-272087 [34]; 93-280630 [35]; 93-361517 [46]; 93-406317 [51]; 94-057215 [07]; 94-281939 [35]; 95-007865 [02]; 95-035631 [05]; 95-253875 [32]; 95-254410 [33]; 95-276487 [37]; 95-365233 [46]; 96-116282 [12]; 96-187653 [19]
DNC C88-142414
TI Rapidly dissolving pharmaceutical compsns. - comprise medicament incorporated in spun fibres of **water** soluble carrier.
DC A96 B07 F01
IN FUISZ, R C
PA (FUIS-N) FUISZ PHARM LTD; (FUIS-I) FUISZ R C; (FUIS-N) FUISZ PHARM LTD
CYC 17
PI WO 8808298 A 881103 (8845)* EN 30 pp
RW: AT BE CH DE FR GB IT LU NL SE
W: AU BR HU JP KR SU
US 4855326 A 890808 (8939) 9 pp
ADT WO 8808298 A WO 88-US1199 880414; US 4855326 A US 88-169838 880318
PRAI US 88-169838 880318; US 87-40371 870420
AN 88-322646 [45] WPIDS
CR 88-322645 [45]; 90-224510 [29]; 90-320018 [42]; 91-086863 [12]; 91-215173 [29]; 93-145785 [18]; 93-167290 [20]; 93-272087 [34]; 93-280630 [35]; 93-361517 [46]; 93-406317 [51]; 94-057215 [07]; 94-281939 [35]; 95-007865 [02]; 95-035631 [05]; 95-253875 [32]; 95-254410 [33]; 95-276487 [37]; 95-365233 [46]; 96-116282 [12]; 96-187653 [19]
AB WO 8808298 A UPAB: 980812
Pharmaceutical compsns. comprise a medicament (I) distributed on or incorporated in a mass of spun fibres of a **water**-soluble material (II).

Pref. (I) is an analgesic, antihistamine, decongestant, dermatotropic agent, antibiotic or **corticosteroid**. Specified(I) are **acetaminophen** and the anthelmintic diethylcarbamazine citrate. (II) is a **sugar** or a cellulosic material, esp. maltose, **fructose**, **sorbitol**, dextrose, **mannitol**, **sucrose** and/or lactose. The compsns. are produced by melt spinning a combination of (I) and (II). The combination is esp. prepd. by adding granules of (II) to a soln. of (I) and opt. an adhesion promoter (esp. polyvinylpyrrolidone) in a nonsolvent for (II), esp. isopropanol, and drying the mixt. The melt-spun prod. is opt. compacted and subdivided into dosage units.

USE/ADVANTAGE - The compsns. may be used for oral, topical or transdermal admin., or for the prepn. of injection solns. in situ in a 2-compartment syringe. The compsns. dissolve very rapidly in **aq** . vehicle and body fluids, esp. facilitating oral admin. of unpleasant-testing drugs to children and animals.

Dwg.0/0
ABEQ EP 358675 B UPAB: 930923
A spun fibrous cosmetic compsn. comprising a rapidly dissoluble mass of **water** soluble spun fibres of a material capable of being spun into fibres that are readily **water**-soluble, and an effective quantity of an active agent distributed on or incorporated in said fibrous mass where said active agent has cosmetologic activity.

0/0
ABEQ US 4855326 A UPAB: 930923

New spun fibrous pharmaceutical compsn. is mass of **water**-sol. fibres e.g. of **sugar** or cellulosic material, contg. medicament and opt. adhesion promoter (PVPD), melt-spun in candyfloss machine above M.Pt. of **sugar** but below that of medicament, then compacted into individual dosage forms, which dissolves quickly on contact with **water**, giving rapid entry by various routes, p.o., topical, systemic and non-systemic, i.v., i.m., by infusion, via multicameral containers, topically by use of wafer of fibres secured to skin.

Pref. **sugar** is 10% lactoase:90% **sucrose**.

Medicaments include analgesics, histaminics, labrinthine depressants, decongectants, dermatopics, acetominophen, diethylcarbazine citrate, **corticosteroids**, dimenhydrimite. Prepn. is by coating granules of **sugar** or methyl cellulose with slurry of medicment e.g. 60-70% soln. in isopropanol contg. 2-3% PVPD to intermediate prod. which is melt-spun.

ADVANTAGE - Very convenient esp. for oral uptake of medicaments.

ABEQ EP 357665 B UPAB: 940418

A dry medicinal disease form comprising a medicament bearing carrier agent

characterised in that the dosage from is prepared by subjecting the carrier agent and the medicament to conditions created in cotton candy spinning equipment to render the carrier agent readily **water**-soluble.

Dwg.0/0

=> d bib abs l65 1-6

L65 ANSWER 1 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 94126267 EMBASE
DN 1994126267
TI Human acute toxicity prediction of the first 50 meic chemicals by a battery of ecotoxicological tests and physicochemical properties.
AU Calleja M.C.; Persoone G.; Geladi P.
CS Research Group for Chemometrics, Institute of Chemistry, University of Umea,Umea, Sweden
SO Food and Chemical Toxicology, (1994) 32/2 (173-187).
ISSN: 0278-6915 CODEN: FCTOD7
CY United Kingdom
DT Journal; Article
FS 046 Environmental Health and Pollution Control
052 Toxicology
037 Drug Literature Index
LA English
SL English
AB Five acute bioassays consisting of three cyst-based tests (with Artemia salina, Streptocephalus proboscideus and Brachionus calyciflorus), the Daphnia magna test and the bacterial luminescence inhibition test (Photobacterium phosphoreum) are used to determine the acute toxicity of the 50 priority chemicals of the Multicentre Evaluation of In Vitro Cytotoxicity (MEIC) programme. These tests and five physicochemical properties (n-octanol- **water** partition coefficient, molecular weight, melting point, boiling point and density) are evaluated either singly or in combination to predict human acute toxicity. Acute toxicity in humans is expressed both as oral lethal doses (HLD) and as lethal concentrations (HLC) derived from clinical cases. A comparison has also been made between the individual tests and the conventional rodent tests, as well as between rodent tests and the batteries resulting from partial least squares (PLS), with regard to their predictive power for acute toxicity in humans. Results from univariate regression show that the predictive potential of bioassays (both ecotoxicological and rodent tests) is generally superior to that of individual physicochemical properties for HLD. For HLC prediction, however, no consistent trend could be discerned that indicated whether bioassays are better estimators than physicochemical parameters. Generally, the batteries resulting from PLS regression seem to be more predictive than rodent tests or any of the individual tests. Prediction of HLD appears to be dependent on the phylogeny of the test species: cructaceans, for example, appear to be more important components in the test battery than rotifers and bacteria. For HLC prediction, one anostracan and one cladoceran crustacean are considered to be important. When considering both ecotoxicological tests and physicochemical properties, the battery based on the molecular weight and the cladoceran crustacean predicts HLC substantially better than any other combination.

L65 ANSWER 2 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 86170011 EMBASE
DN 1986170011
TI Dosage recommendations for activated charcoal-**sorbitol** treatment.
AU Minocha A.; Krenzelok E.P.; Spyker D.A.

CS Department of Internal Medicine, University of Virginia Medical Center, Charlottesville, VA 22908, United States
SO Journal of Toxicology - Clinical Toxicology, (1985) 23/7-8 (579-587). CODEN: JTCTDW
CY United States
DT Journal
FS 037 Drug Literature Index
052 Toxicology
030 Pharmacology
LA English
AB Activated charcoal-**sorbitol** mixture is used for the treatment of acute poisoning. Based on our experience with healthy adults, overdosed patients and published reports, we have devised a protocol for use of this mixture in different concentrations of **sorbitol**. The dose is based on the size of the patient, type of poison, and the clinical status.
In seriously ill adult patients, we recommend the use of 1 g/kg of activated charcoal in 4.3 ml/kg body weight of 70% **sorbitol** every 4 hours until the first stool containing charcoal appears. In children and ambulatory adults, the same dose of activated charcoal may be administered in 4.3 ml/kg body weight of 35% **sorbitol**. Patients requiring multple doses may be administered activated charcoal as **aqueous** and **sorbitol** suspensions alternately every 2-6 hours after the first charcoal stool has appeared. The patients on multiple dose regimen, especially children, should be closely monitored for any fluid or electrolyte imbalance or depletion of essential vitamins.

L65 ANSWER 3 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 86123538 EMBASE
DN 1986123538
TI Investigation of auranofin-induced diarrhoea.
AU Behrens R.; Devereaux M.; Hazleman B.; et al.
CS Department of Gastroenterology, Addenbrooke's Hospital, Cambridge CB2 1QE, United Kingdom
SO Gut, (1986) 27/1 (59-65). CODEN: GUTTAK
CY United Kingdom
DT Journal
FS 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
031 Arthritis and Rheumatism
030 Pharmacology
LA English
AB Gastrointestinal function was assessed in six patients with rheumatoid arthritis who had developed diarrhoea on treatment with Auranofin. With the administration of Auranofin whole gut transit time decreased markedly (to 50% or less of control values) in five of six patients. The speed of passage of intestinal contents through the colon was certainly increased but attempts transit through the upper gastrointestinal tract failed because the breath hydrogen method gave inconclusive results. There was no evidence of colitis and in all cases biopsy of the rectal mucosa appeared normal by light microscopy. In the five patients with rapid intestinal transit faecal weight increased more than two-fold (range +44 to +335%)

although in only three cases were the changes sufficient to cause an increased frequency of bowel action. Overall the concentration of sodium in faecal **water** increased three-fold (mean values rose from 10.6 to 38.3 mmol/l). There were no significant changes in the concentrations of either potassium or chloride but bicarbonate was reduced. Faecal pH fell from a mean value of 7.5 (range 6.8-7.9) to a mean value of 6.4 (range 6.0-7.4). In the three patients who developed overt diarrhoea and in two others taking Auranofin the intestinal uptake of 51Cr-EDTA was increased on average three-fold and there was a similar change in the ratio of the absorption of lactulose/**mannitol**. The mean clearance of alpha-1-antitrypsin from the circulation into the gastrointestinal tract was doubled. These data indicate an increase in intestinal permeability. In contrast the absorption of vitamin B12 was unaffected and there was no significant change in the excretion of faecal fat although one patient developed mild steatorrhoea. Thus in a selected group of subjects with rheumatoid arthritis the administration of Auranofin caused diarrhoea in association with a reversible defect in intestinal permeability but without significant change in the absorption of nutrients.

L65 ANSWER 4 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 83103551 EMBASE
DN 1983103551
TI Drug induced changes in **water** excretion.
AU Gardenswartz M.H.; Berl T.
CS Dep. Med., Univ. Colorado Health Sci. Cent., Denver, CO 80262, United States
SO Kidney, (1981) 14/1 (19-23).
CODEN: KIDNAI
CY United States
DT Journal
FS 038 Adverse Reactions Titles
037 Drug Literature Index
028 Urology and Nephrology
018 Cardiovascular Diseases and Cardiovascular Surgery
003 Endocrinology
006 Internal Medicine
007 Pediatrics and Pediatric Surgery
LA English

L65 ANSWER 5 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 82174099 EMBASE
DN 1982174099
TI [Intoxication by **water** and antidiuresis conditions].
LES INTOXICATIONS PAR L'EAU ET LES ETATS D'ANTIDIURESE.
AU Rince M.; Charmes J.P.; Leroux-Robert C.
CS Serv. Nephrol., CHU Dupuytren, 87000 Limoges, France
SO Revue du Praticien, (1982) 32/21 (1427-1439).
CODEN: REPRA3
CY France
DT Journal
FS 038 Adverse Reactions Titles
037 Drug Literature Index
003 Endocrinology
028 Urology and Nephrology
LA French
SL English

L65 ANSWER 6 OF 6 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.

AN 81110922 EMBASE
DN 1981110922
TI Specific modalities of therapy for inappropriate antidiuretic hormone secretion.
AU Sordillo P.; Matarese R.A.; Novich R.K.; et al.
CS Nephrol. Sect., Dept. Med., Lenox Hill Hosp., New York, N.Y. 10021, United States
SO Clinical Nephrology, (1981) 15/3 (107-110).
CODEN: CLNHBI
CY Germany
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
LA English
AB In addition to general therapeutic maneuvers which will correct hypoosmolality in all patients with SIADH, there also exist precise remedies which can successfully treat SIADH in a specific manner. When the diagnosis of SIADH is made, general measures such as **water** restriction and salt replacement should be started, and more vigorous therapeutic maneuvers such as the use of concentrated salt solutions and diuretics should be considered. In addition, however, consideration must also be given to the specific type of SIADH that is to be treated. As illustrated, if endogenous excessive ADH secretion has resulted either from a drug which stimulates ADH release, or from stimuli arising elsewhere in the organism such as may occur with extensive pulmonary or central nervous system disease, use of an agent which can suppress ADH secretion, such as phenytoin, in usual doses, should be considered. Furthermore, if SIADH secondary to neoplasm is encountered, the use of demeclocycline, an agent which blocks ADH effect at the level of the collecting tubule, will prove most efficacious. This agent may be used in low doses for extended periods of time if necessary, if careful follow-up for evidence of renal, or other, toxicity is made. Finally, the diagnosis of **glucocorticoid** deficiency should always be considered when SIADH is encountered since this disorder can be rapidly corrected by **glucocorticoid** administration. In addition, this diagnosis may also alert the physician to the possibility of other serious hormone deficiencies.

=> D BIB ABS HITRN L36

L36 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel **stable** liquid injectable paracetamol compositions
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805314	A1	19980212	WO 97-FR1452	19970805
	W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2751875	A1	19980206	FR 96-9858	19960805
	FR 2751875	B1	19981224		
	CA 2233924	AA	19980212	CA 97-2233924	19970805
	AU 9739451	A1	19980225	AU 97-39451	19970805
	EP 858329	A1	19980819	EP 97-936739	19970805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FR 96-9858	19960805			
	WO 97-FR1452	19970805			

AB Novel **stable** paracetamol compns. for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The compns. contain a soln. of paracetamol in an **aq**. solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq** . solvent to remove oxygen from the medium. Said compns. may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable compns. for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol compns.)

=> D BIB ABS HITRN L44 1-2

L44 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel **stable** liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9805314	A1	19980212	WO 97-FR1452	19970805
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2751875	A1	19980206	FR 96-9858	19960805
FR 2751875	B1	19981224		
CA 2233924	AA	19980212	CA 97-2233924	19970805
AU 9739451	A1	19980225	AU 97-39451	19970805
EP 858329	A1	19980819	EP 97-936739	19970805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 96-9858 19960805
WO 97-FR1452 19970805

AB Novel **stable** paracetamol **compns.** for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns.** contain a soln. of paracetamol in an **aq.** solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq.** solvent to remove oxygen from the medium. Said **compns.** may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns.** for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol **compns.**)

L44 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 1999 ACS
AN 1983:192833 HCAPLUS
DN 98:192833
TI Retention behavior of drugs and metabolites in **aqueous** two-phase liquid chromatography system employing silica gel support
AU Hara, Shoji; Ijitsu, Takanori; Matsumoto, Takeshi
CS Tokyo Coll. Pharm., Hachioji, 192-03, Japan
SO Yakugaku Zasshi (1983), 103(2), 240-4
CODEN: YKKZAJ; ISSN: 0031-6903

DT Journal
LA Japanese
AB The retention indexes of 16 drugs and metabolites including hypnotics, antiepileptics, analgesics, and **central nervous system** stimulants in liq. chromatog. were systematically examd. to devise a highly efficient extn. and fractionation procedure for biol. fluid anal. A high-performance system incorporating an acid-treated silica gel column and a UV detector was used to det. the capacity ratios in **aq**. biphasic solvents contg. various ratios of Et2O and hexane (1:0, 7:3, 1:1, 3:7) as the org. phase. The cor. capacity ratios were calcd. from the exptl. retention data and phase ratios. A linear correlation was found between the log of the cor. capacity ratio value and the log of solvent **compn**. in a liq.-liq. partition system.
IT **103-90-2**
RL: ANT (Analyte); ANST (Analytical study)
(chromatog. of, high-performance liq., with biphasic solvents, for biol. fluid anal.)

=> D BIB ABS HITRN L50

L50 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:198226 HCAPLUS
DN 128:196658
TI Pharmaceutical **compositions** containing benzodiazepines, antipyretics, and benzoic acid **stabilizers**
IN Besse, Jerome
PA Laboratoires Crinex, Fr.
SO Fr. Demande, 14 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2747923	A1	19971031	FR 96-5259	19960425
FR 2747923	B1	19980717		

AB Pharmaceutical **compns.** contg. benzodiazepines, antipyretics, and benzoic acid **stabilizers** are claimed for the treatment of convulsions in infants. A pharmaceutical **compn.** contained flunitrazepam 0.02, paracetamol 10, sodium benzoate 10, Cremophor RH40 5, PEG-400 18, glycerol 14.6, Lycasin 80/55, sodium saccharinate 5.5, sorbic acid 0.135, POBMS 0.07, POBPS 0.03, citric acid 0.075, trisodium citrate 0.36, PVP K17 0.36, colors 0.0008, fragrance 1.8 g, and **water** q.s. 100 mL.
IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **compns.** contg. benzodiazepines, antipyretics, and benzoic acid **stabilizers**)

=> D BIB ABS HITRN L50 2-9

L50 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel **stable** liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9805314	A1	19980212	WO 97-FR1452	19970805
W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2751875	A1	19980206	FR 96-9858	19960805
FR 2751875	B1	19981224		
CA 2233924	AA	19980212	CA 97-2233924	19970805
AU 9739451	A1	19980225	AU 97-39451	19970805
EP 858329	A1	19980819	EP 97-936739	19970805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
PRAI FR 96-9858 19960805
WO 97-FR1452 19970805
AB Novel **stable** paracetamol **compns.** for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns.** contain a soln. of paracetamol in an **aq.** solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq.** solvent to remove oxygen from the medium. Said **compns.** may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns.** for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.
IT **103-90-2**, Paracetamol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol **compns.**)

L50 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:172582 HCAPLUS
DN 126:176681
TI **Stable** cosmetic **compositions** containing surfactants and fatty alcohols
IN Wagner, Julie Ann; Zukowski, Joseph Michael; Robinson, Larry Richard; Deckner, George Endel; Rinaldi, Marie Antoinette; Szymanski, Victoria Claire
PA Procter & Gamble Company, USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9701326	A1	19970116	WO 96-US10940	19960626
	W: AU, CA, CN, CZ, JP, KR, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2225444	AA	19970116	CA 96-2225444	19960626
	AU 9663968	A1	19970130	AU 96-63968	19960626
	EP 835095	A1	19980415	EP 96-923465	19960626
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRAI US 95-673 19950629
US 95-2170 19950811
US 96-647083 19960508
WO 96-US10940 19960626
OS MARPAT 126:176681
AB The present invention relates to leave on, skin care **compns.**, comprising (A) from about 0.001% to about 20% of an active ingredient, (B) from about 1% to about 20% of a **stable**, hydrophobic, structuring agent selected from the group consisting of satd. C16-30 fatty alcs., satd. C16-30 fatty alcs. contg. from about 1-5 mol of ethylene oxide,

satd. C16-30 diols, satd. C16-30 monoglycerol ethers, satd. C16-30 hydroxy fatty acids, and **mixts.** thereof, having a m.p. of at least about 45.degree.; and (C) from about 0.05 to about 10% of a hydrophilic surfactant selected from the group consisting of anionic surfactants, cationic surfactants, zwitterionic surfactants, and **mixts.** thereof; and (D) from about 25% to about 98.949% **water.** These **compns.** are useful for delivering a wide variety of active ingredients to the skin. Thus, a moisturizing oil-in-**water** emulsion contained salicylic acid 2, PPG Bu ether 8.00, glycerin 4.00, stearyl alc. 1.5, cetyl alc. 3.00, distearyldimethylammonium chloride 0.1, propylene glycol 3.00, Steareth-21 2.0, Steareth-2 1.0, Dimethicone 1.0, cyclomethicone 1.0, disodium EDTA 0.02, and **water** qs 100%.

IT **103-90-2**, Acetaminophen
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**stable** cosmetic **compns.** contg. surfactants and fatty alcs.)

L50 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:926443 HCAPLUS
DN 123:321729
TI Low pH, hydrolytically **stable**, cosmetic **compositions** containing acidic actives
IN Deckner, George Endel; Rinaldi, Marie Antoinette; Szymanski, Victoria Claire
PA Procter and Gamble Co., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524179	A1	19950914	WO 95-US2840	19950307
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UG, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2185231	AA	19950914	CA 95-2185231	19950307
	AU 9519825	A1	19950925	AU 95-19825	19950307
	EP 748203	A1	19961218	EP 95-912775	19950307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1145582	A	19970319	CN 95-192519	19950307
	JP 09510208	T2	19971014	JP 95-523594	19950307
	US 5824666	A	19981020	US 95-576264	19951221
PRAI	US 94-212413		19940311		
	WO 95-US2840		19950307		

OS MARPAT 123:321729
AB The present invention relates to leave on, oil-in-**water**, skin care **compns.** comprising (1) 0.05-20% of an acidic active ingredient, preferably having a soly. parameter of 6-12; (2) 0.1-25% of alkoxylated alcs., alkoxylated polyols, and **mixts.** thereof; (3) 1-20% of an acid **stable**, hydrophobic structuring agent selected from the group consisting of satd. C16-30 fatty alcs., satd. C16-30 fatty alcs. contg. 1-5 mol of ethylene oxide, satd. C16-30 diols, satd. C16-30

monoglycerol ethers, satd. C16-30 hydroxy fatty acids, and **mixts**. thereof, having a m.p. of .gtoreq.45.degree.; (4) 0.05-10% of an acid **stable**, hydrophilic surfactant selected from the group consisting of anionic, cationic, zwitterionic, nonionic surfactant, and **mixts**. thereof; and (5) 25-99.7% **water**, wherein the pH of the **compn**. is .ltoreq.3.5. These cosmetic **compns**. provide improved phys. and chem. **stability**, while providing good skin deposition and good skin penetration of the active ingredients, while also providing low dermal irritation. An oil-in-**water** emulsion moisturizer contained salicylic acid 2, PPG-14 Bu ether 8, glycerin 4, stearyl alc. 1.5, cetyl alc. 3, distearyldimethylammonium chloride 0.1, propylene glycol 3, steareth-21 2, steareth-2 1, dimethicone 1, cyclomethicone 1, di-Na EDTA 0.02, minor ingredients 0.07, and **water** to 100%.

IT **103-90-2**, Acetaminophen
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** topical **compns**. contg. acidic actives for desquamation and moisturization)

L50 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:613011 HCAPLUS
DN 121:213011
TI Cold/sinus preparation consisting of phenindamine tartrate
IN Lech, Stanley; Weng, Timothy H.
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9418970	A1	19940901	WO 94-US378	19940111
	W: AU, CA, JP, NZ				
	RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9460867	A1	19940914	AU 94-60867	19940111
PRAI	US 93-18981		19930218		
	WO 94-US378		19940111		

AB An improved pharmaceutical **compn**. useful in the treatment of cold, sinus and allergies comprises a chem. unstable antihistamine such as phenindamine that is **stabilized** in a non-**aq**., inert carrier system. More specifically, the phenindamine is **stabilized** in a mineral oil/fumed silica particle matrix and other active drugs such as analgesics, decongestants and expectorants can be incorporated for a more effective, multi-system formula. For example, capsules were manufd. from a **mixt**. contg. PEG 101.6, phenindamine tartrate 10.0, Cabosil silica gel 8.0, and pseudoephedrine HCl 24.0 g.

IT **103-90-2**, Acetaminophen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules contg. phenindamine and therapeutic agents for treatment of sinus and allergy and cold symptoms)

L50 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1993:66861 HCAPLUS
DN 118:66861
TI **Stable** suspension **formulations** for controlled drug

delivery
IN Chang, Nienyuan J.
PA Allergan, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9211871	A1	19920723	WO 91-US9480	19911217
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MW, NO, RO, SD, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
US 5275820	A	19940104	US 90-634500	19901227
AU 9191306	A1	19920817	AU 91-91306	19911217
EP 564537	A1	19931013	EP 92-902222	19911217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06504051	T2	19940512	JP 91-502746	19911217
PRAI US 90-634500	19901227			
WO 91-US9480	19911217			

AB Sustained-release pharmaceuticals are prepd. by incorporating small ion-exchange resin particles in microcapsules (prior to incorporation in a polymer matrix) and utilizing these microcapsules in liq. suspensions. The **compns.** have improved drug delivery properties and long-term storage **stability.** Thus, 0.2 g Bio-Rad AG50W-X8 was added to 10 mL **aq.** soln. of levobunolol-HCl and filtered. The drug-bound resin was dried and suspended in 50 mL MeCN soln. of poly(methyl vinyl ether-maleic anhydride) (60%). Sep., 1.5 g poly(vinylpyrrolidone) (mol. wt. 22,000) was dissolved in 25 mL MeCN and the resulting soln. was added to the resin. A white matrix ppt. with resin particles embedded in it was formed. The ppt. was washed with MeCN and dried. The final drug content in the polymer matrix was 8.5% (by wt.). In pH 7.4 buffer, a drug release of >6 h was obsd.
IT **103-90-2**
RL: BIOL (Biological study)
(sustained-release suspension for, polymers and ion exchangers in)

L50 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1987:623295 HCAPLUS
DN 107:223295
TI Phenindamine-based pharmaceutical **compositions** for treatment of sinusitis, allergy, and common cold
IN Shtohryn, Liudoslava V.; Liudoslava, V. Shtohryn; Peters, David; David, Peters
PA Warner-Lambert Co., USA
SO S. African, 23 pp.
CODEN: SFXXAB
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ZA 8605923	A	19870325	ZA 86-5923	19860806
US 4820523	A	19890411	US 86-852471	19860415

	DK 8603727	A	19871016	DK 86-3727	19860805
	DK 166756	B1	19930712		
	AU 8661137	A1	19871022	AU 86-61137	19860812
	AU 569431	B2	19880128		
	FI 8603362	A	19871016	FI 86-3362	19860820
	JP 62242619	A2	19871023	JP 86-194137	19860821
	JP 06021067	B4	19940323		
	ES 2001391	A6	19880516	ES 86-1304	19860822
	CA 1267605	A1	19900410	CA 86-516666	19860822
	EP 241615	A1	19871021	EP 86-307609	19861002
	EP 241615	B1	19910918		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 67407	E	19911015	AT 86-307609	19861002
PRAI	US 86-852471	19860415			
	EP 86-307609	19861002			

AB The title pharmaceutical **compns.** contain a phenindamine (I) salt within a leachable nontoxic wax matrix in addn. to .gtoreq.1 materials chosen from an analgesic, a decongestant, and/or an antitussive. A **compn.** consisting of I 25, wax 40, and CaSO4 20 wt.% was dry blended with acetaminophen and pseudoephedrine and compressed to tablets (contg. I 23, pseudoephedrine 5.5, and acetaminophen 58%), and stored at 25, 45, and 60.degree. for 1 mo. The tablets exhibited good **stability** with no isomerization at 25.degree. and 45.degree.; storage at 60.degree. resulted in 15% conversion. In addn., the tablets exhibited 88.8% dissoln. into **water** after 1 h stirring 50 rpm at 37.degree..

IT **103-90-2**
RL: BIOL (Biological study)
(pharmaceuticals contg. phenindamine salt and, for treatment of sinusitis and allergy and cold)

L50 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1986:39771 HCAPLUS
DN 104:39771
TI Directly compressible pharmaceutical **compositions**
IN Salpekar, Anil; Haag, Thomas E.
PA Mallinckrodt, Inc., USA
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 159852	A2	19851030	EP 85-302470	19850409
	EP 159852	A3	19870520		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	CA 1261260	A1	19890926	CA 85-478481	19850404
PRAI	US 84-600809	19840416			

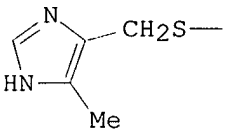
AB A compressible pharmaceutical **compn.** contains an interactive compd. such as codeine, a binder such as poly(vinylpyrrolidone), and a filler such as lactose. The **compn.** is granulated and dry-blended with another analgesic, such as aspirin, acetaminophen, **ibuprofen**, etc. The **mixt.** can be tableted. As opposed to wet tableting, intimate contact between the active ingredients is avoided by this method, and product **stability** is increased. Thus, 6000 g codeine phosphate, 5520 g lactose, and 480 g poly(vinylpyrrolidone) were granulated using abs. EtOH as a solvent. The granules were dried. The granules (120 mg) were tableted with 325 mg

aspirin in the usual manner. The tablets (581.65 mg) remained white after
3 mo of storage, whereas tablets of similar **compn.**, prepd. by **water**-granulation, yellowed after 2 wk.
IT **103-90-2**
RL: BIOL (Biological study)
(tablet contg. codeine and, dry granulation process for)

L50 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 1999 ACS
AN 1980:75900 HCAPLUS
DN 92:75900
TI 1,2-Substituted 3-cyanoguanidines
IN Ballester Rodes, Montserrat; Palomo Nicolau, Claudio; Palomo Coll, Antonio
Luis
PA Spain
SO Span., 21 pp.
CODEN: SPXXAD
DT Patent
LA Spanish
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 472001	A1	19790716	ES 78-472001	19780724

GI



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AB Cyanoguanidines RNHC(:NCN)NHR1 [I, R, R1 = C1-C6 alkyl or cycloalkyl or aryl, optionally substituted with HS, Cl, Br, or heterocyclyl (e.g., Q) groups] were prepd. by treating carbodiimides RN:C:NR1 with 1-4 equiv NCNH2 in MeCN, DMF, AcNMe, Me2SO, 1,4-dioxane, or their **mixts.** with **H2O** and heating at 90-160.degree.. Under the reaction conditions, the carbodiimides are **stabilized** as salts with NCNH2. Thus, refluxing N,N'-dicyclohexylcarbodiimide and NCNH2 in DMF for
60 min followed by cooling and addn. of **H2O** gave 92% I (R = R1 = cyclohexyl). This compd. was not formed after 52 h in Et2O contg. anhyd. Na2SO4. Also prepd. were I (R = Me, R1 = Bu, QCH2CH2, Ph, ClCH2CH2, hexyl; R = R1 = Ph).
IT **103-90-2**
RL: RCT (Reactant)
(esterification of, with (thenoylphenyl)propionyl chloride)

=> D BIB ABS HITRN L66 1-3

L66 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel **stable** liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805314	A1	19980212	WO 97-FR1452	19970805
	W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2751875	A1	19980206	FR 96-9858	19960805
	FR 2751875	B1	19981224		
	CA 2233924	AA	19980212	CA 97-2233924	19970805
	AU 9739451	A1	19980225	AU 97-39451	19970805
	EP 858329	A1	19980819	EP 97-936739	19970805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FR 96-9858	19960805			
	WO 97-FR1452	19970805			

AB Novel **stable** paracetamol **compns.** for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns.** contain a soln. of paracetamol in an **aq.** solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq.** solvent to remove oxygen from the medium. Said **compns.** may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns.** for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **50-70-4**, Glucitol, biological studies **50-81-7D**, Ascorbic acid, alk. earth metal salts **50-81-7D**, Ascorbic acid, derivs. **50-99-7**, Glucose, biological studies **56-81-5**, Glycerol, biological studies **57-27-2**, Morphine, biological studies **57-48-7**, Levulose, biological studies **57-55-6**, Propylene glycol, biological studies **69-65-8**, Mannitol **87-89-8**, Inositol **96-27-5**, .alpha.-Thioglycerol **103-90-2**, Paracetamol **134-03-2**, Sodium ascorbate **3483-12-3**, Dithiothreitol **6055-06-7**, Morphine hydrochloride trihydrate **10504-35-5D**, D-Ascorbic acid, derivs. **25322-68-3**, Peg **62624-30-0D**, Ascorbic acid, alkali metal salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol **compns.**)

L66 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:34823 HCAPLUS
DN 124:97765
TI Controlled-release **formulations** coated with **aqueous** dispersions of ethylcellulose
IN Oshlack, Benjamin; Chasin, Mark; Pedi, Frank Jr.
PA Euroceltique, S.A., Luxembourg
SO U.S., 47 pp. Cont.-in-part of U.S. 5,273,760.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5472712	A	19951205	US 93-81618	19930623
	US 5273760	A	19931228	US 91-814111	19911224
	ZA 9201366	A	19921230	ZA 92-1366	19920225
	CA 2061824	AA	19930625	CA 92-2061824	19920225
	IL 101080	A1	19961205	IL 92-101080	19920227
	JP 07165609	A2	19950627	JP 92-71808	19920330
	IN 173298	A	19940326	IN 92-CA462	19920629
	BR 9202982	A	19930629	BR 92-2982	19920731
	AU 9230024	A1	19930701	AU 92-30024	19921208
	AU 652871	B2	19940908		
	NO 9205016	A	19930625	NO 92-5016	19921223
	EP 630646	A1	19941228	EP 94-109115	19940614
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2125904	AA	19941224	CA 94-2125904	19940615
	AU 9464846	A1	19950119	AU 94-64846	19940620
	AU 680491	B2	19970731		
	FI 9403022	A	19941224	FI 94-3022	19940622
	NO 9402382	A	19941227	NO 94-2382	19940622
	JP 07138189	A2	19950530	JP 94-142012	19940623
	JP 08175977	A2	19960709	JP 94-221510	19940916
	AU 9743687	A1	19980122	AU 97-43687	19971031
PRAI	US 91-814111	19911224			
	US 93-81618	19930623			

AB A **stabilized** solid controlled-release **formulation**, having a coating derived from an **aq**. dispersion of a hydrophobic polymer, is obtained by overcoating a substrate including an active agent with an **aq**. dispersion of the plasticized hydrophobic polymer and then curing the coated substrate at a temp. above the glass transition temp. of the plasticized hydrophobic polymer. Curing is continued to an endpoint at which the coated substrate provides **stabilized** dissoln. of the active agent, which is unchanged after exposure to accelerated storage conditions. The endpoint is detd. by comparing the dissoln. profile of the **formulation** immediately after curing to the dissoln. profile after exposure to accelerated storage conditions of .gtoreq.1 mo at 37.degree. and relative humidity 80%. The active agent may be a systemically or locally active therapeutic agent, disinfecting and sanitizing agent, cleansing agent, fragrance agent, or fertilizing agent. Thus, Nu Pariel 18/20 beads were spray coated with an **aq**. soln. of hydromorphone-HCl and Opadry Y-5-1442 (contg. hydroxypropylmethylcellulose, hydroxypropylcellulose, TiO2, and PEG) and then given an overcoating of Opadry Y-5-1442, coated with Aquacoat (plasticized ethylcellulose), cured at 60.degree. and various relative

humidities for 24 or 72 h, and overcoated with Opadry Y-5-1442 to reduce agglomeration. Conditions of curing (accelerated storage) had little effect on the dissoln. behavior in gastric juice.

IT **57-27-2**, Morphine, biological studies **64-31-3**, Morphine sulfate **103-90-2**, Acetaminophen **509-60-4**, Dihydromorphine **52485-79-7**, Buprenorphine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release **formulations** coated with **aq.** dispersions of ethylcellulose)

IT **9004-64-2**, Hydroxypropylcellulose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release **formulations** coated with **aq.** dispersions of ethylcellulose)

IT **63-42-3**, Lactose **9004-65-3**, Hydroxypropylmethylcellulose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(release-modifying coating; controlled-release **formulations** coated with **aq.** dispersions of ethylcellulose)

L66 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 1999 ACS
AN 1984:145003 HCAPLUS
DN 100:145003
TI Controlled release oral **mixtures** containing microencapsulated pharmaceuticals
IN Kallstrand, Anders Goran Vilhelm; Mattsson, Kjell Johan; Sjoqvist, Rolf Ivar
PA Astra Lakemedel AB, Swed.
SO Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2122490	A1	19840118	GB 83-17071	19830623
	GB 2122490	B2	19860403		
	IL 68779	A1	19871231	IL 83-68779	19830525
	ZA 8303931	A	19840725	ZA 83-3931	19830530
	CA 1214726	A1	19861202	CA 83-429157	19830530
	EP 101418	A2	19840222	EP 83-850147	19830531
	EP 101418	A3	19841114		
	EP 101418	B1	19901227		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 59286	E	19910115	AT 83-850147	19830531
	DK 8302723	A	19831225	DK 83-2723	19830614
	DK 161365	B	19910701		
	DK 161365	C	19911209		
	FI 8302197	A	19831225	FI 83-2197	19830616
	FI 85213	B	19911213		
	FI 85213	C	19920325		
	AU 8315943	A1	19840105	AU 83-15943	19830620
	AU 561954	B2	19870521		
	NO 8302293	A	19831227	NO 83-2293	19830623
	NO 168745	B	19911223		
	NO 168745	C	19920401		
	JP 59016822	A2	19840128	JP 83-111990	19830623
	JP 05059089	B4	19930830		

	HU 29576	O	19840228	HU 83-2225	19830623
	HU 189300	B	19860630		
	ES 523536	A1	19840401	ES 83-523536	19830623
	DD 209971	A5	19840530	DD 83-252303	19830623
	CS 257769	B2	19880615	CS 83-4636	19830623
	SU 1722207	A3	19920323	SU 83-3607650	19830623
	US 4994260	A	19910219	US 85-815125	19851230

PRAI SE 82-3953 19820624
US 82-383148 19820525
EP 83-850147 19830531
US 83-500618 19830603
US 84-668168 19841111

AB The release of an encapsulated pharmaceutical is controlled, any unpleasant taste is masked, and the active ingredient is **stabilized** by the presence of 40-99% of a carbohydrate or a carbohydrate-related compd. The dry powder is dissolved or suspended in an **aq**. soln. before oral administration. Drug release from the microcapsules in the soln. or suspension (leakage) is very low but release in the body is rapid. Thus, $NaHCO_3$ 0.83, mannitol [**69-65-8**] 9.35, and sucrose [**57-50-1**] 83.1 g were mixed and then blended with 5.61 g of an Et cellulose [9004-57-3]-microencapsulated bacampicillin-HCl [37661-08-8] prepn. contg. 70% drug. The powder, 4.81 g, was added to 5 mL **H2O** to give a **mixt**. contg. 46% by wt. of release-controlling carbohydrates. Drug release from the microcapsules in the **mixt**. was 0.5% in 1 day and 1.2% in 10 days. Release into **H2O** was 60% in 0.042 day and 90% in 0.084 day.

IT **103-90-2 114-07-8**
RL: BIOL (Biological study)
(microencapsulated, drug release control in **aq**. suspensions of, by carbohydrates)

IT **50-70-4**, biological studies **50-99-7**, biological studies **56-81-5**, biological studies **57-48-7**, biological studies **57-50-1**, biological studies **69-65-8 87-99-0**
RL: BIOL (Biological study)
(pharmaceutical release control by, from microcapsules in **aq**. suspensions)

IT **25322-68-3**
RL: USES (Uses)
(pharmaceutical release control by, from microcapsules in **aq**. suspensions)

=> D L65 BIB ABS HITSTR

L65 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 1999 ACS
AN 1999:7930 HCAPLUS
DN 130:49527
TI Chemistry control in clinical chemistry assays
IN Peddicord, Julie; Kang, Douglas; Clark, Douglas; Puia, Angela
PA Medical Analysis Inc., USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9856719	A2	19981217	WO 98-US10513	19980521

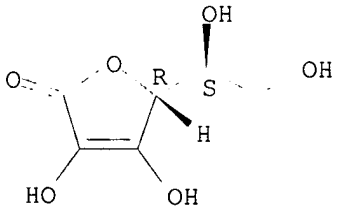
W: CN, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 97-874383 19970613

AB **Stabilized compns.** for use in clin. chem. assays are disclosed. The **compn.** is **stable** in the liq. form. The **compn.** minimizes the use of human derived starting materials and uses recombinant thermophilic enzymes as a substitute for native enzymes commonly used in chem. controls. A stock buffer soln. was prepd. from bis Tris propane, protease-free bovine serum albumin, NaCl, protease-free IgG (the IgG is omitted if recombinant thermophilic acid phosphatase is used), .beta.-cyclodextrin, Tween-20, cholesterol, and **water.**

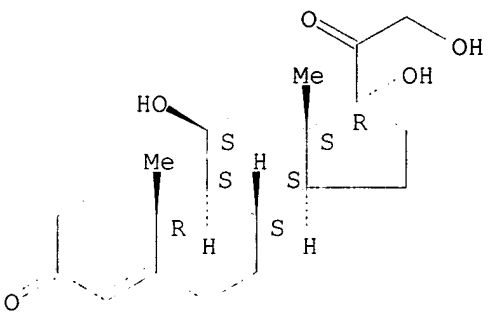
IT **50-81-7**, Ascorbic acid, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(base matrix contg.; chem. control in clin. chem. assays)
RN 50-81-7 HCAPLUS
CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



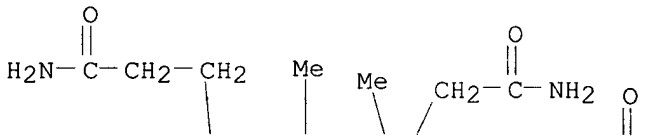
IT **50-23-7**, Cortisol **68-19-9**, Vitamin B12
20830-75-5, Digoxin
RL: ANT (Analyte); ARU (Analytical role, unclassified); ANST (Analytical study)
(chem. control in clin. chem. assays)
RN 50-23-7 HCAPLUS
CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

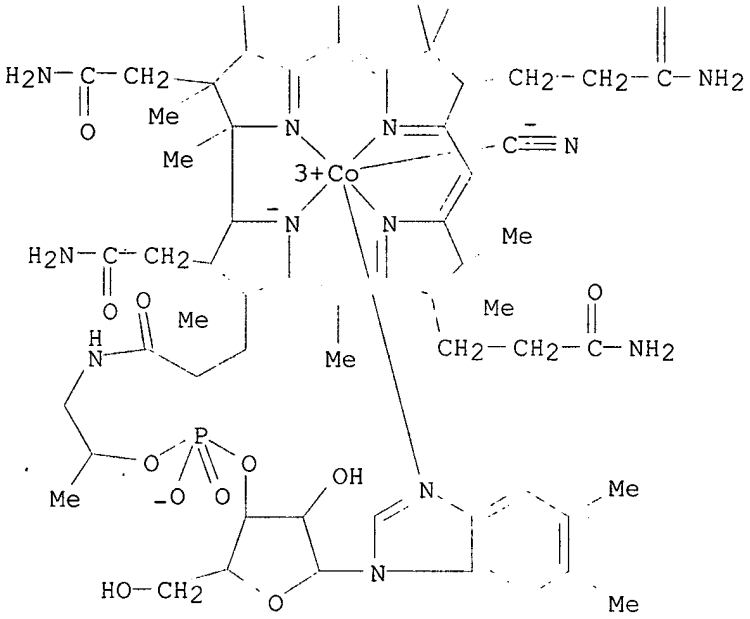


RN 68-19-9 HCAPLUS
CN Vitamin B12 (8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

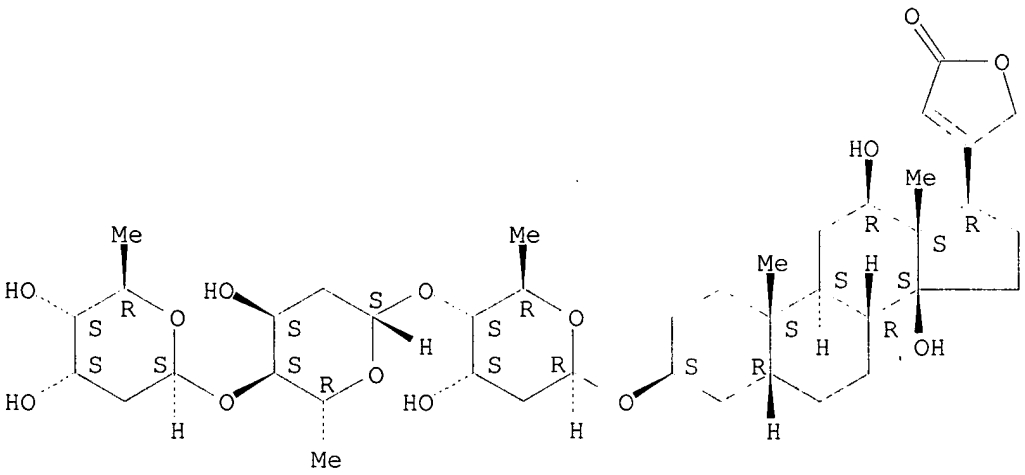


PAGE 2-A



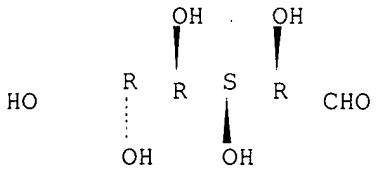
RN 20830-75-5 HCAPLUS
CN Card-20(22)-enolide, 3-[(O-2,6-dideoxy-.beta.-D-ribo-hexopyranosyl-(1.fwdarw.4)-O-2,6-dideoxy-.beta.-D-ribo-hexopyranosyl-(1.fwdarw.4)-2,6-dideoxy-.beta.-D-ribo-hexopyranosyl)oxy]-12,14-dihydroxy-, (3.beta.,5.beta.,12.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

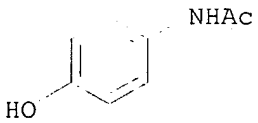


IT **50-99-7**, Glucose, analysis
RL: ANT (Analyte); ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)
(chem. control in clin. chem. assays)
RN 50-99-7 HCAPLUS
CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



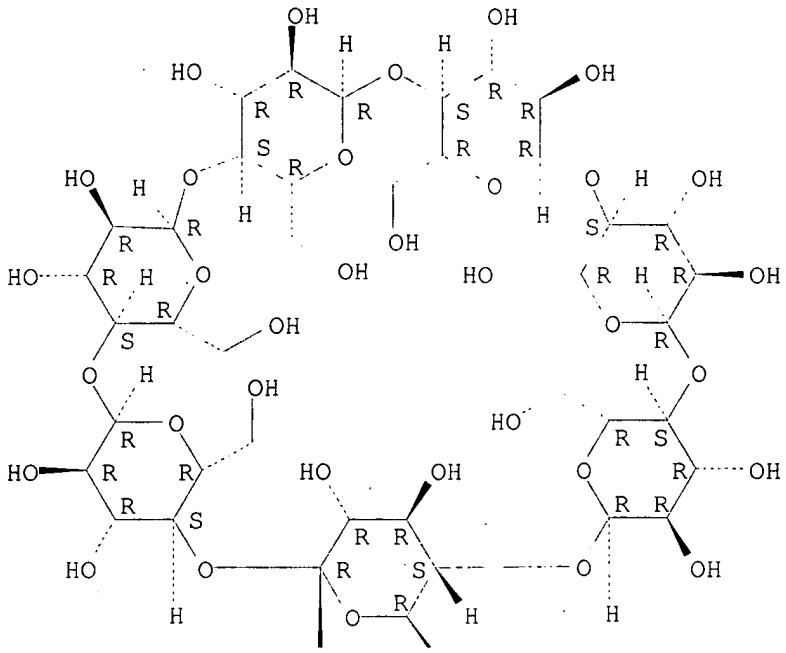
IT **103-90-2**, Acetaminophen
RL: ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)
(**stability** of, in liq. chem. control; chem. control in clin. chem. assays)
RN 103-90-2 HCAPLUS
CN Acetamide, N-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



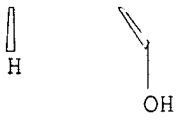
IT **7585-39-9**, .beta.-Cyclodextrin **64431-96-5**, Bis Tris propane
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(stock buffer soln. contg.; chem. control in clin. chem. assays)
RN 7585-39-9 HCAPLUS
CN .beta.-Cyclodextrin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

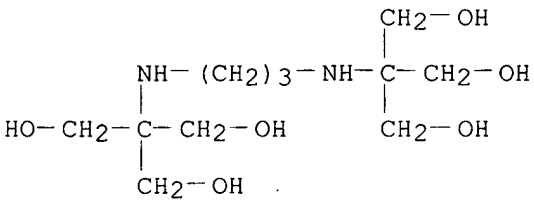
PAGE 1-A



PAGE 2-A



RN 64431-96-5 HCAPLUS
CN 1,3-Propanediol, 2,2'-(1,3-propanediyldiimino)bis[2-(hydroxymethyl)-
(9CI)
(CA INDEX NAME)



=> D L65 BIB ABS HITSTR 2-3

L65 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:34823 HCAPLUS
DN 124:97765
TI Controlled-release **formulations** coated with **aqueous** dispersions of ethylcellulose
IN Oshlack, Benjamin; Chasin, Mark; Pedi, Frank Jr.
PA Euroceltique, S.A., Luxembourg
SO U.S., 47 pp. Cont.-in-part of U.S. 5,273,760.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5472712	A	19951205	US 93-81618	19930623
	US 5273760	A	19931228	US 91-814111	19911224
	ZA 9201366	A	19921230	ZA 92-1366	19920225
	CA 2061824	AA	19930625	CA 92-2061824	19920225
	IL 101080	A1	19961205	IL 92-101080	19920227
	JP 07165609	A2	19950627	JP 92-71808	19920330
	IN 173298	A	19940326	IN 92-CA462	19920629
	BR 9202982	A	19930629	BR 92-2982	19920731
	AU 9230024	A1	19930701	AU 92-30024	19921208
	AU 652871	B2	19940908		
	NO 9205016	A	19930625	NO 92-5016	19921223
	EP 630646	A1	19941228	EP 94-109115	19940614
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2125904	AA	19941224	CA 94-2125904	19940615
	AU 9464846	A1	19950119	AU 94-64846	19940620
	AU 680491	B2	19970731		
	FI 9403022	A	19941224	FI 94-3022	19940622
	NO 9402382	A	19941227	NO 94-2382	19940622
	JP 07138189	A2	19950530	JP 94-142012	19940623
	JP 08175977	A2	19960709	JP 94-221510	19940916
	AU 9743687	A1	19980122	AU 97-43687	19971031
PRAI	US 91-814111	19911224			
	US 93-81618	19930623			

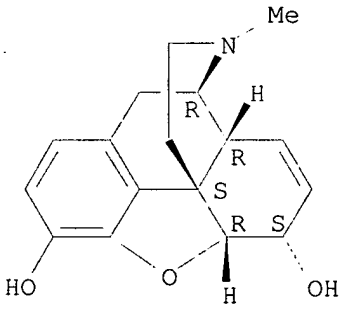
AB A **stabilized** solid controlled-release **formulation**, having a coating derived from an **aq**. dispersion of a hydrophobic polymer, is obtained by overcoating a substrate including an active agent with an **aq**. dispersion of the plasticized hydrophobic polymer and then curing the coated substrate at a temp. above the glass transition temp. of the plasticized hydrophobic polymer. Curing is continued to an endpoint at which the coated substrate provides **stabilized** dissoln. of the active agent, which is unchanged after exposure to accelerated storage conditions. The endpoint is detd. by comparing the dissoln. profile of the **formulation** immediately after curing to the dissoln. profile after exposure to accelerated storage conditions of .gtoreq.1 mo at 37.degree. and relative humidity 80%. The active agent may be a systemically or locally active therapeutic agent, disinfecting and sanitizing agent, cleansing agent, fragrance agent, or fertilizing agent. Thus, Nu Pariel 18/20 beads were spray coated with an **aq** . soln. of hydromorphone-HCl and Opadry Y-5-1442 (contg.

hydroxypropylmethylcellulose, hydroxypropylcellulose, TiO2, and PEG) and then given an overcoating of Opadry Y-5-1442, coated with Aquacoat (plasticized ethylcellulose), cured at 60.degree. and various relative humidities for 24 or 72 h, and overcoated with Opadry Y-5-1442 to reduce agglomeration. Conditions of curing (accelerated storage) had little effect on the dissoln. behavior in gastric juice.

IT **57-27-2**, Morphine, biological studies **64-31-3**, Morphine sulfate **103-90-2**, Acetaminophen **509-60-4**, Dihydromorphine **52485-79-7**, Buprenorphine
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release **formulations** coated with **aq.** dispersions of ethylcellulose)

RN 57-27-2 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

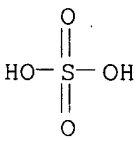
Absolute stereochemistry.



RN 64-31-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5.alpha.,6.alpha.)-, sulfate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

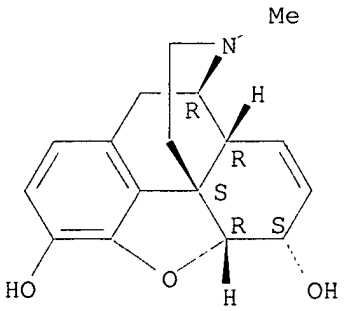
CRN 7664-93-9
CMF H2 O4 S



CM 2

CRN 57-27-2
CMF C17 H19 N O3
CDES 4:5A,6A.MORPHINAN..5

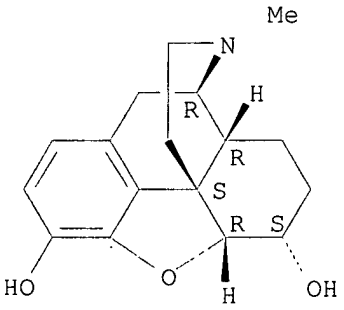
Absolute stereochemistry.



RN 103-90-2 HCAPLUS
CN Acetamide, N-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

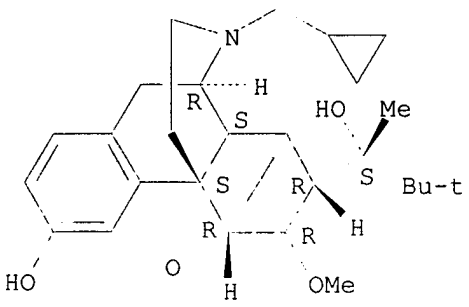
RN 509-60-4 HCAPLUS
CN Morphinan-3,6-diol, 4,5-epoxy-17-methyl-, (5.alpha.,6.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 52485-79-7 HCAPLUS
CN 6,14-Ethenomorphinan-7-methanol, 17-(cyclopropylmethyl)-.alpha.-(1,1-dimethylethyl)-4,5-epoxy-18,19-dihydro-3-hydroxy-6-methoxy-.alpha.-methyl-, (.alpha.S,5.alpha.,7.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **9004-64-2**, Hydroxypropylcellulose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release **formulations** coated with **aq.** dispersions of ethylcellulose)
RN 9004-64-2 HCAPLUS
CN Cellulose, 2-hydroxypropyl ether (9CI) (CA INDEX NAME)

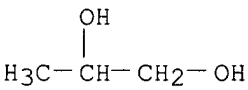
CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

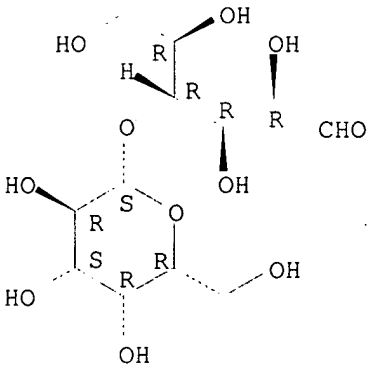
CM 2

CRN 57-55-6
CMF C3 H8 O2



IT **63-42-3**, Lactose **9004-65-3**, Hydroxypropylmethylcellulose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(release-modifying coating; controlled-release **formulations** coated with **aq.** dispersions of ethylcellulose)
RN 63-42-3 HCAPLUS
CN D-Glucose, 4-O-.beta.-D-galactopyranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 9004-65-3 HCAPLUS
CN Cellulose, 2-hydroxypropyl methyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

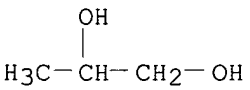
CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

CM 3

CRN 57-55-6
CMF C3 H8 O2



L65 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 1999 ACS
AN 1989:179558 HCAPLUS
DN 110:179558
TI Preparation of inclusion compounds of cyclodextrin ethers with lipophilic drugs
IN Pitha, Josef
PA United States Dept. of Health and Human Services, USA
SO U.S., 7 pp. Cont.-in-part of U.S. 4,596,795.
CODEN: USXXAM
DT Patent

LA English
FAN.CNT 2

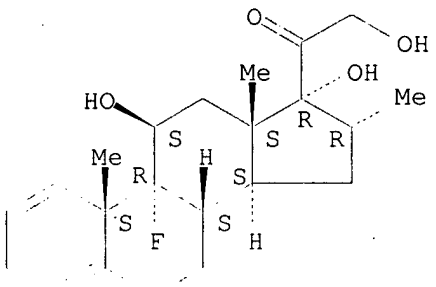
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4727064	A	19880223	US 85-738749	19850529
	US 603839	A0	19840831	US 84-603839	19840425
	US 4596795	A	19860624		
PRAI	US 84-603839	19840425			

AB Inclusion compds. of a cyclodextrin-based **mixt.** and a drug with a substantially low **water**-soly., are prepd. to improve dissoln. properties of the drug and hence its absorption by the body. Hydroxypropyl .beta.-cyclodextrin was prepd. by treating .beta.-cyclodextrin with propylene oxide in alk. media. The soly. of estradiol in **aq.** soln. contg. 40% hydroxypropyl .beta.-cyclodextrin was 28.0, compared to <1.6 mg/mL in **water.** Hydroxypropyl .beta.-cyclodextrin with medium degrees of substitution (5-7) was more effective solubilizer than that of higher degrees of substitution. The solns. of drugs in cyclodextrins were **stable** when kept at room temp. for several months and no microbial growth in the solns. was obsd.

IT **50-02-2DP**, Dexamethasone, complexes with hydroxypropyl .beta.-cyclodextrin **50-28-2DP**, Estra-1,3,5(10)-triene-3,17-diol (17.beta.)-, complexes with cyclodextrin ethers **58-00-4DP**, Apomorphine, complexes with hydroxypropyl .beta.-cyclodextrin **103-90-2DP**, Acetaminophen, complexes with hydroxypropyl .beta.-cyclodextrin **630-60-4DP**, complexes with hydroxypropyl .beta.-cyclodextrin **7585-39-9DP**, .beta.-Cyclodextrin, hydroxypropyl ethers, complexes with lipophilic drugs **10016-20-3DP**, .alpha.-Cyclodextrin, hydroxypropyl ethers, complexes with lipophilic drugs **17465-86-0DP**, .gamma.-Cyclodextrin, hydroxypropyl ethers, complexes with lipophilic drugs **20830-75-5DP**, complexes with hydroxypropyl .beta.-cyclodextrin
RL: PREP (Preparation)
(prepn. of, drug soly. enhancement by)

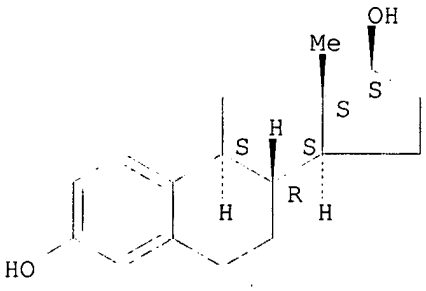
RN 50-02-2 HCAPLUS
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



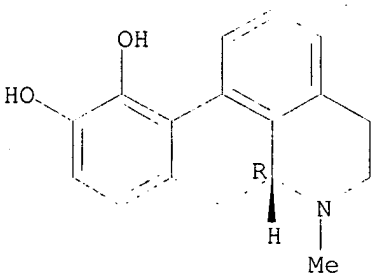
RN 50-28-2 HCAPLUS
CN Estra-1,3,5(10)-triene-3,17-diol (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

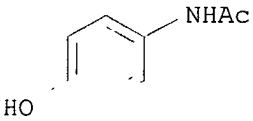


RN 58-00-4 HCAPLUS
CN 4H-Dibenzo[de,g]quinoline-10,11-diol, 5,6,6a,7-tetrahydro-6-methyl-, (6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

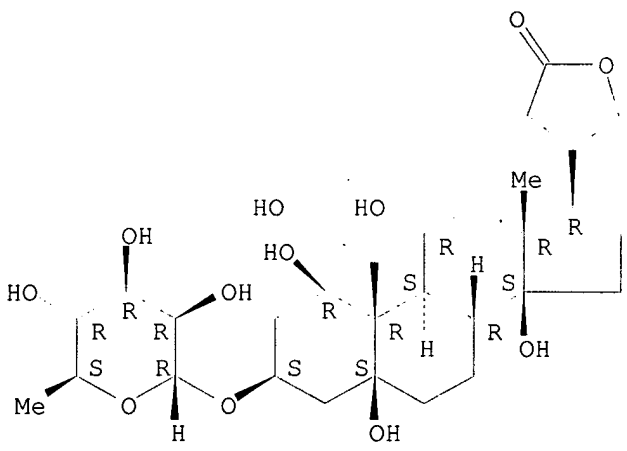


RN 103-90-2 HCAPLUS
CN Acetamide, N-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 630-60-4 HCAPLUS
CN Card-20(22)-enolide, 3-[(6-deoxy-.alpha.-L-mannopyranosyl)oxy]-1,5,11,14,19-pentahydroxy-, (1.beta.,3.beta.,5.beta.,11.alpha.)- (9CI) (CA INDEX NAME)

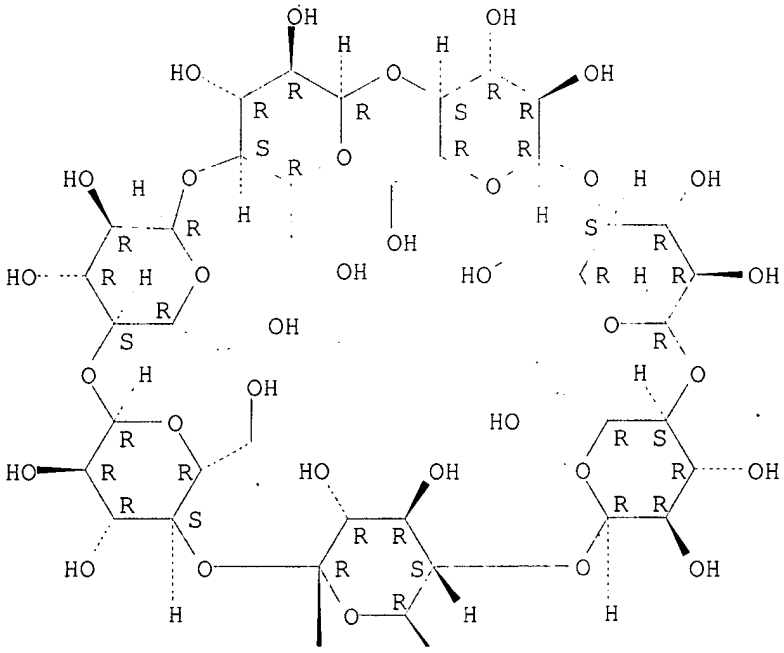
Absolute stereochemistry.



RN 7585-39-9 HCAPLUS
CN .beta.-Cyclodextrin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

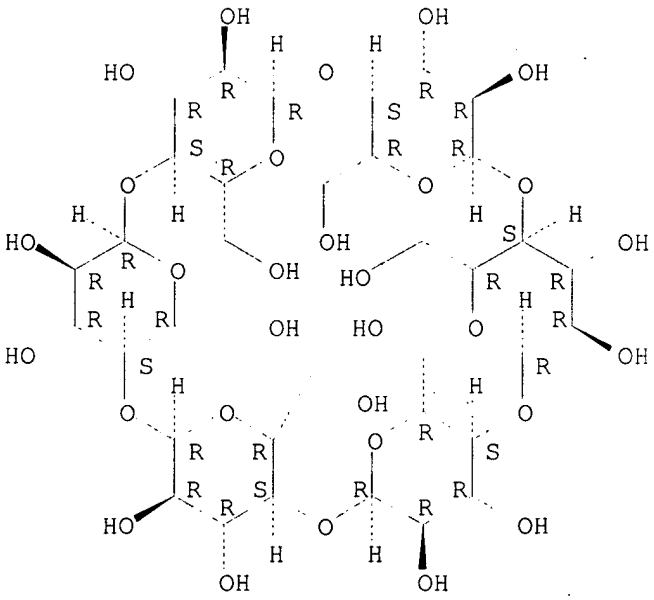
PAGE 1-A



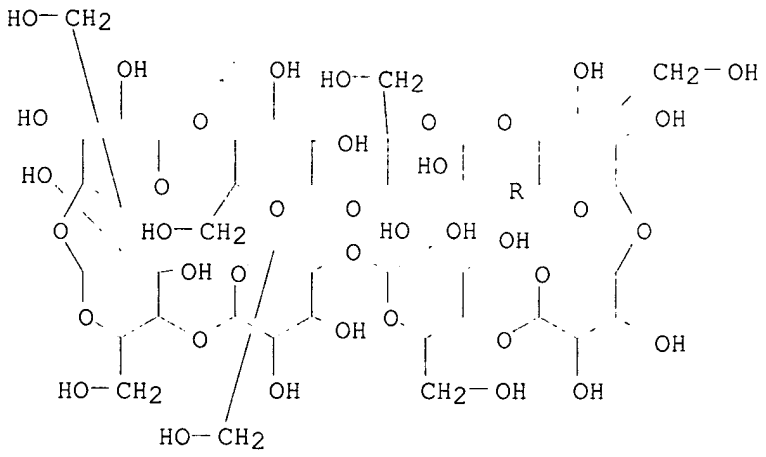
PAGE 2-A

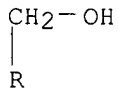
RN 10016-20-3 HCAPLUS
CN .alpha.-Cyclodextrin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



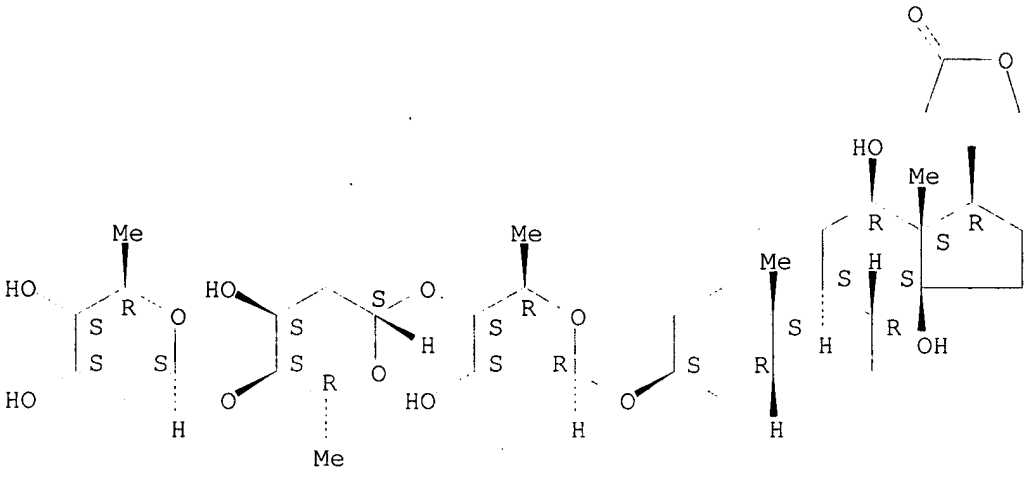
RN 17465-86-0 HCAPLUS
CN .gamma.-Cyclodextrin (8CI, 9CI) (CA INDEX NAME)



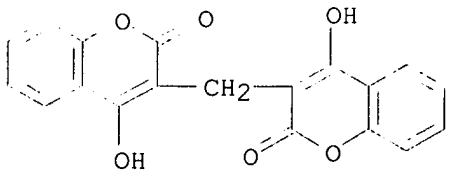


RN 20830-75-5 HCAPLUS
CN Card-20(22)-enolide, 3-[(O-2,6-dideoxy-.beta.-D-ribo-hexopyranosyl-(1.fwdarw.4)-O-2,6-dideoxy-.beta.-D-ribo-hexopyranosyl-(1.fwdarw.4)-2,6-dideoxy-.beta.-D-ribo-hexopyranosyl)oxy]-12,14-dihydroxy-, (3.beta.,5.beta.,12.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **66-76-2DP**, complexes with cyclodextrin ethers
RL: PREP (Preparation)
(prepn. of, drug soly. enhancement in)
RN 66-76-2 HCAPLUS
CN 2H-1-Benzopyran-2-one, 3,3'-methylenebis[4-hydroxy- (9CI) (CA INDEX NAME)


O
O
OH
CH2
OH
O
O

=> D BIB ABS HITRN L72

L72 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel **stable** liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805314	A1	19980212	WO 97-FR1452	19970805
	W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2751875	A1	19980206	FR 96-9858	19960805
	FR 2751875	B1	19981224		
	CA 2233924	AA	19980212	CA 97-2233924	19970805
	AU 9739451	A1	19980225	AU 97-39451	19970805
	EP 858329	A1	19980819	EP 97-936739	19970805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 96-9858 19960805
WO 97-FR1452 19970805

AB Novel **stable** paracetamol **compns.** for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns.** contain a soln. of paracetamol in an **aq.** solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A **water**-insol. inert gas is carefully bubbled through the **aq.** solvent to remove oxygen from the medium. Said **compns.** may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns.** for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **50-70-4**, Glucitol, biological studies **50-81-7D**, Ascorbic acid, alk. earth metal salts **50-81-7D**, Ascorbic acid, derivs. **50-99-7**, Glucose, biological studies **56-81-5**, Glycerol, biological studies **57-27-2**, Morphine, biological studies **57-48-7**, Levulose, biological studies **57-55-6**, Propylene glycol, biological studies **69-65-8**, Mannitol **87-89-8**, Inositol **96-27-5**, .alpha.-Thioglycerol **103-90-2**, Paracetamol **134-03-2**, Sodium ascorbate **3483-12-3**, Dithiothreitol **6055-06-7**, Morphine hydrochloride trihydrate **10504-35-5D**, D-Ascorbic acid, derivs. **25322-68-3**, Peg **62624-30-0D**, Ascorbic acid, alkali metal salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel **stable** liq. injectable paracetamol **compns.**)

=> D BIB ABS HITRN L72 2-5

L72 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:172582 HCAPLUS
DN 126:176681
TI **Stable** cosmetic **compositions** containing surfactants and fatty alcohols
IN Wagner, Julie Ann; Zukowski, Joseph Michael; Robinson, Larry Richard; Deckner, George Endel; Rinaldi, Marie Antoinette; Szymanski, Victoria Claire
PA Procter & Gamble Company, USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9701326	A1	19970116	WO 96-US10940	19960626
	W: AU, CA, CN, CZ, JP, KR, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2225444	AA	19970116	CA 96-2225444	19960626
	AU 9663968	A1	19970130	AU 96-63968	19960626
	EP 835095	A1	19980415	EP 96-923465	19960626
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRAI US 95-673 19950629
US 95-2170 19950811
US 96-647083 19960508
WO 96-US10940 19960626
OS MARPAT 126:176681
AB The present invention relates to leave on, skin care **compns.**, comprising (A) from about 0.001% to about 20% of an active ingredient, (B) from about 1% to about 20% of a **stable**, hydrophobic, structuring agent selected from the group consisting of satd. C16-30 fatty alcs., satd. C16-30 fatty alcs. contg. from about 1-5 mol of ethylene oxide, satd. C16-30 diols, satd. C16-30 monoglycerol ethers, satd. C16-30 hydroxy fatty acids, and **mixts.** thereof, having a m.p. of at least about 45.degree.; and (C) from about 0.05 to about 10% of a hydrophilic surfactant selected from the group consisting of anionic surfactants, cationic surfactants, zwitterionic surfactants, and **mixts.** thereof; and (D) from about 25% to about 98.949% **water**. These **compns.** are useful for delivering a wide variety of active ingredients to the skin. Thus, a moisturizing oil-in-**water** emulsion contained salicylic acid 2, PPG Bu ether 8.00, glycerin 4.00, stearyl alc. 1.5, cetyl alc. 3.00, distearyldimethylammonium chloride 0.1, propylene glycol 3.00, Steareth-21 2.0, Steareth-2 1.0, Dimethicone 1.0, cyclomethicone 1.0, disodium EDTA 0.02, and **water** qs 100%.
IT **50-23-7**, **Hydrocortisone** **60-54-8**, Tetracycline **96-26-4**, Dihydroxyacetone **103-90-2**, Acetaminophen **108-46-3**, 1,3-Benzenediol, biological studies **25322-68-3D**, fatty ethers
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(**stable** cosmetic **compns**. contg. surfactants and fatty alcs.)

L72 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:926443 HCAPLUS
DN 123:321729
TI Low pH, hydrolytically **stable**, cosmetic **compositions** containing acidic actives
IN Deckner, George Endel; Rinaldi, Marie Antoinette; Szymanski, Victoria Claire
PA Procter and Gamble Co., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524179	A1	19950914	WO 95-US2840	19950307
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UG, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2185231	AA	19950914	CA 95-2185231	19950307
	AU 9519825	A1	19950925	AU 95-19825	19950307
	EP 748203	A1	19961218	EP 95-912775	19950307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1145582	A	19970319	CN 95-192519	19950307
	JP 09510208	T2	19971014	JP 95-523594	19950307
	US 5824666	A	19981020	US 95-576264	19951221
PRAI	US 94-212413	19940311			
	WO 95-US2840	19950307			

OS MARPAT 123:321729
AB The present invention relates to leave on, oil-in-**water**, skin care **compns**. comprising (1) 0.05-20% of an acidic active ingredient, preferably having a soly. parameter of 6-12; (2) 0.1-25% of alkoxylated alcs., alkoxylated polyols, and **mixts**. thereof; (3) 1-20% of an acid **stable**, hydrophobic structuring agent selected from the group consisting of satd. C16-30 fatty alcs., satd. C16-30 fatty alcs. contg. 1-5 mol of ethylene oxide, satd. C16-30 diols, satd. C16-30 monoglycerol ethers, satd. C16-30 hydroxy fatty acids, and **mixts**. thereof, having a m.p. of .gtoreq.45.degree.; (4) 0.05-10% of an acid **stable**, hydrophilic surfactant selected from the group consisting of anionic, cationic, zwitterionic, nonionic surfactant, and **mixts**. thereof; and (5) 25-99.7% **water**, wherein the pH of the **compn**. is .ltoreq.3.5. These cosmetic **compns**. provide improved phys. and chem. **stability**, while providing good skin deposition and good skin penetration of the active ingredients, while also providing low dermal irritation. An oil-in-**water** emulsion moisturizer contained salicylic acid 2, PPG-14 Bu ether 8, glycerin 4, stearyl alc. 1.5, cetyl alc. 3, distearyldimethylammonium chloride 0.1, propylene glycol 3, steareth-21 2, steareth-2 1, dimethicone 1, cyclomethicone 1, di-Na EDTA 0.02, minor ingredients 0.07, and **water** to 100%.
IT **50-23-7**, **Hydrocortisone 56-81-5**, Glycerin,

biological studies **57-55-6**, Propylene glycol, biological studies **60-54-8**, Tetracycline **96-26-4**, Dihydroxyacetone **103-90-2**, Acetaminophen **108-46-3**, Resorcinol, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** topical **compns**. contg. acidic actives for desquamation and moisturization)

L72 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1989:484108 HCAPLUS
DN 111:84108
TI Pharmaceuticals containing spun sugar fibers as solid carriers
IN Fuisz, Richard C.
PA USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8808298	A1	19881103	WO 88-US1199	19880414
	W: AU, BR, HU, JP, KR, SU				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4855326	A	19890808	US 88-169838	19880318
	IL 86053	A1	19910916	IL 88-86053	19880413
	AU 8817104	A1	19881202	AU 88-17104	19880414
	AU 609137	B2	19910426		
	EP 357665	A1	19900314	EP 88-904094	19880414
	EP 357665	B1	19940302		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03500164	T2	19910117	JP 88-503773	19880414
	HU 54491	A2	19910328	HU 88-3238	19880414
	HU 207941	B	19930728		
	AT 102021	E	19940315	AT 88-904094	19880414
	RU 2056835	C1	19960327	RU 88-4742414	19880414
	CA 1315679	A1	19930406	CA 88-564394	19880418
	ZA 8802770	A	19881228	ZA 88-2770	19880420
	ZA 8802771	A	19881228	ZA 88-2771	19880420
	WO 9107952	A1	19910613	WO 90-US6093	19901024
	W: AU, BR, HU, JP, KR, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9066488	A1	19910626	AU 90-66488	19901024
	AU 640966	B2	19930909		
	EP 502865	A1	19920916	EP 90-916659	19901024
	EP 502865	B1	19950906		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	BR 9007887	A	19920929	BR 90-7887	19901024
	IL 96199	A1	19941128	IL 90-96199	19901031
	CA 2029175	AA	19910531	CA 90-2029175	19901101
	CA 2029175	C	19960521		
	ZA 9009092	A	19910925	ZA 90-9092	19901113
	CA 2141909	AA	19950811	CA 95-2141909	19950206
	EP 667147	A2	19950816	EP 95-650004	19950208
	EP 667147	A3	19960424		
	R: BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
	JP 08038138	A2	19960213	JP 95-43651	19950209
	CN 1119934	A	19960410	CN 95-102933	19950210

PRAI US 87-40371 19870420
US 88-169838 19880318
EP 88-904094 19880414
WO 88-US1199 19880414
US 89-444045 19891130
WO 90-US6093 19901024
US 94-194682 19940210

AB A pharmaceutical comprises a mass of spun fibers of a material that is readily **water**-sol. and a pharmacol. active agent distributed throughout the fibrous mass. A slurry contg. 60-70% wt./vol. acetaminophen and iso-PrOH was mixed with granular sugar and the granules were uniformly coated with the slurry, dried for 3-4 h at 45-65.degree., and the dried granules were converted to fibers on a conventional cotton candy machine to give a pediatric **formulation**. The pharmaceutical had the appearance of cotton candy and contained 87.0-91.0% by wt. acetaminophen. The material is compacted preferably to a wafer-like structure while avoiding fracturing the fibers and retaining the fibrous character in order to ensure rapid dissoln. in saliva or in a solvent; the **compn**. is packaged in a moisture-proof package or wrapper. Sucrose is susceptible to deterioration in the presence of moisture, however the inclusion of 10% by wt. lactose gives a more **stable** product; lactose absorbs moisture and acts as desiccant. Spinning of a **mixt**. of 10% flavored lactose and sucrose at the temp. required for spinning sucrose results in a **compn**. wherein the lactose is uniformly dispersed throughout the fibrous mass. Lactose alone is a good carrier, with or without sweetener, and removes the unpleasant aftertaste of the drug.

IT **57-50-1**, biological studies
RL: BIOL (Biological study)
(fiber, as pharmaceutical carriers)

IT **50-70-4**, Sorbitol, biological studies **50-99-7**, D-Glucose, biological studies **57-48-7**, Fructose, biological studies **63-42-3**, Lactose **69-65-8**, Mannitol **69-79-4**, Maltose
RL: BIOL (Biological study)
(fibers, as pharmaceutical carriers)

IT **103-90-2**, Acetaminophen **2375-03-3**, Methylprednisolone sodium succinate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg., sugar fibers as carriers for)

L72 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1988:498644 HCAPLUS
DN 109:98644
TI Grinding effect on some pharmaceutical properties of drugs by adding .beta.-cyclodextrin
AU Lin, Shan Yang; Kao, Yuh Horng; Yang, Juei Chyi
CS Dep. Med. Res., Veterans Gen. Hosp., Taipei, Taiwan
SO Drug Dev. Ind. Pharm. (1988), 14(1), 99-118
CODEN: DDIPD8; ISSN: 0363-9045
DT Journal
LA English
AB The effect of grinding on the physicochem. properties of ground **mixts**. of cryst. drugs (acetaminophen, warfarin, indomethacin, diazepam and **hydrocortisone** acetate) with .beta.-cyclodextrin was studied by IR anal., x-ray diffraction and thermal anal. The crystallinities of drugs decreased with increasing grinding time and became amorphous or nearly amorphous, which depended on drug moiety and

cavity size of .beta.-cyclodextrin. Acetaminophen became amorphous and only formed an inclusion complex in the ground **mixt.** with .beta.-cyclodextrin, although all 5 drugs interacted with .beta.-cyclodextrin in **water.** The dissoln rate of drugs from the ground **mixts.** were higher than that of the ground drug, cryst. drug or phys. **mixt.**, while the dissoln. rate of the inclusion complex was the very highest. Physicochem. **stability** of the ground **mixts.** stored <40.degree. and 75% relative humidity condition was measured by DSC. In the case of diazepam, indomethacin, warfarin or **hydrocortisone** acetate and .beta.-cyclodextrin ground **mixt.**, drug was crystd. and the crystallinity increased with an increase of storage time, which reached an equil. state after 15 days-storage. However, acetaminophen-.beta.-cyclodextrin ground **mixt.** was still amorphous during 60 days-storage.

IT **7585-39-9**, .beta.-Cyclodextrin
RL: BIOL (Biological study)
(drugs physicochem. properties in relation to grinding with)

IT **76992-01-3**
RL: FORM (Formation, nonpreparative)
(formation of, in ground **mixts.**)

IT **50-03-3**, **Hydrocortisone** acetate **103-90-2**, Acetaminophen
RL: PRP (Properties)
(physicochem. properties of, grinding with .beta.-cyclodextrin effect on)

=> D BIB ABS HITRN L78

L78 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:293427 HCAPLUS
DN 129:8597
TI Embedding and encapsulation of controlled release particles
IN Van Lengerich, Bernhard H.
PA Van Lengerich, Bernhard H., USA
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9818610	A1	19980507	WO 97-US18984	19971027
	W: AU, CA, JP, NO, PL, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9749915	A1	19980522	AU 97-49915	19971027
PRAI	US 96-29038		19961028		
	US 97-52717		19970716		
	WO 97-US18984		19971027		

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high **water** binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as **water**, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temp. of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable **mixt**. The **mixt**. is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

IT **50-02-2**, Dexamethasone **50-23-7**, Hydrocortisone **50-24-8**, Prednisolone **50-27-1**, Estriol **50-28-2**, Estradiol, biological studies **50-58-8**, Phendimetrazine tartrate **50-81-7**, Ascorbic acid, biological studies **50-96-4**, Isoetharine hydrochloride **51-30-9**, Isoproterenol hydrochloride **51-43-4**, Epinephrine **53-03-2**, Prednisone **56-53-1**, Diethylstilbestrol **56-75-7**, Chloramphenicol **57-22-7**, Vincristine **57-63-6**, Ethinyl

estradiol **57-92-1**, Streptomycin, biological studies **58-00-4**, Apomorphine **58-32-2**, Dipyridamole **58-56-0**, Pyridoxine hydrochloride **59-92-7**, Levodopa, biological studies **60-54-8**, Tetracycline **61-76-7**, Phenylephrine hydrochloride **62-31-7**, Dopamine hydrochloride **62-67-9**, Nalorphine **64-31-3**, Morphine sulfate **64-72-2**, Chlortetracycline hydrochloride **66-76-2**, Dicoumarol **67-73-2**, Fluocinolone acetonide **68-19-9**, Cyanocobalamin **71-63-6**, Digitoxin **76-43-7**, Fluoxymesterone **77-09-8** **79-57-2**, Oxytetracycline **80-53-5**, Terpin **81-13-0**, Dexpanthenol **83-43-2**, Methylprednisolone **83-88-5**, Riboflavin, biological studies **84-17-3**, Dienestrol **93-14-1**, Guaifenesin **103-90-2**, Acetaminophen **108-46-3**, Resorcinol, biological studies **114-07-8**, Erythromycin **115-77-5**, Pentaerythritol, biological studies **123-31-9**, Hydroquinone, biological studies **124-94-7**, Triamcinolone **125-72-4**, Levorphanol tartrate **127-33-3**, Demeclocycline **128-46-1** , Dihydrostreptomycin **134-03-2**, Sodium ascorbate **136-77-6**, Hexylresorcinol **143-71-5**, Hydrocodone bitartrate **152-97-6**, Fluocortolone **299-27-4**, Potassium gluconate **299-29-6**, Ferrous gluconate **304-59-6**, Potassium sodium tartrate **329-65-7**, 1,2-Benzenediol, 4-[1-hydroxy-2-(methylamino)ethyl]- **357-07-3**, Oxymorphone hydrochloride **378-44-9**, Betamethasone **379-79-3**, Ergotamine tartrate **382-67-2**, Desoximetasone **426-13-1**, Fluorometholone **434-07-1**, Oxymetholone **437-74-1**, Xantinol nicotinate **465-65-6**, Naloxone **479-18-5**, Dyphylline **514-36-3**, Fludrocortisone acetate **518-47-8**, Fluorescein sodium **527-07-1**, Sodium gluconate **536-21-0** , Norfenefrine **555-30-6**, Methyldopa **564-25-0**, Doxycycline **579-56-6**, Isoxsuprine hydrochloride **652-67-5** , Isosorbide **709-55-7**, Etilefrine **745-65-3**, Alprostadil **859-18-7**, Lincomycin hydrochloride **865-21-4** , Vinblastine **1070-11-7**, Ethambutol hydrochloride **1098-97-1**, Pyritinol **1143-38-0**, Anthralin **1247-42-3**, Meprednisone **1263-89-4**, Paromomycin sulfate **1393-48-2**, Thiostrepton **1404-93-9**, Vancomycin hydrochloride **1476-53-5**, Novobiocin sodium **1524-88-5**, Flurandrenolide **1597-82-6**, Paramethasone acetate **2013-58-3**, Meclocycline **2589-47-1**, Prajmalium bitartrate **2589-47-1**, Prajmalium bitartrate, biological studies **3385-03-3**, Flunisolide **3546-41-6**, Pyrvinium pamoate **3632-91-5**, Magnesium gluconate **3963-95-9**, Methacycline hydrochloride **4330-99-8**, Trimeprazine tartrate **4468-02-4** , Zinc gluconate **5355-48-6** **5536-17-4**, Vidarabine **5874-97-5**, Metaproterenol sulfate **6284-40-8**, Meglumine **7054-25-3**, Quinidine gluconate **7681-93-8**, Natamycin **10246-75-0**, Hydroxyzine pamoate **12650-69-0**, Mupirocin **13292-46-1**, Rifampin **13392-18-2**, Fenoterol **13422-51-0**, Hydroxocobalamin **13614-98-7**, Minocycline hydrochloride **18378-89-7**, Plicamycin **18559-94-9**, Salbutamol **19356-17-3**, Calcifediol **20830-75-5**, Digoxin **21462-39-5**, Clindamycin hydrochloride **22204-24-6**, Pyrantel pamoate **23031-25-6**, Terbutaline **23031-32-5**, Terbutaline sulfate **23214-92-8**, Doxorubicin **23288-49-5** , Probucol **23869-24-1**, O-(.beta.-Hydroxyethyl)-rutoside **24390-14-5**, Doxycycline hyclate **24729-96-2**, Clindamycin phosphate **25322-68-3**, Polyethylene glycol **25389-94-0**,

Kanamycin sulfate **26652-09-5**, Ritodrine **27823-62-7**, Chlortetracycline bisulfate **28860-95-9**, Carbidopa **30685-43-9**, Metildigoxin **32780-64-6**, Labetalol hydrochloride **33402-03-8**, Metaraminol bitartrate **33419-42-0**, Etoposide **36688-78-5 36791-04-5**, Ribavirin **37517-28-5**, Amikacin **42200-33-9**, Nadolol **49745-95-1**, Dobutamine hydrochloride **50679-08-8**, Terfenadine **56392-17-7**, Metoprolol tartrate **58551-69-2** , Carboprost tromethamine **60166-93-0**, Iopamidol **60833-22-9**, Pyridoxal 5'-phosphate glutamate **66108-95-0**, Iohexol **81103-11-9**, Clarithromycin **83905-01-5**, Azithromycin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

=> D BIB ABS HITRN L78 2-10

L78 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:268331 HCAPLUS
DN 128:326507
TI Pharmaceutical **composition** for rapid suspension in **aqueous** media
IN Calanchi, Massimo Maria; Marconi, Marco Giuseppe Raffaele; Mapelli, Luigi Giovanni
PA Eurand International S.P.A., Italy; Calanchi, Massimo Maria; Marconi, Marco Giuseppe Raffaele; Mapelli, Luigi Giovanni
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817250	A1	19980430	WO 97-EP5863	19971023
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	GB 2318511	A1	19980429	GB 96-22090	19961023
	AU 9851887	A1	19980515	AU 98-51887	19971023
PRAI	GB 96-22090	19961023			
	WO 97-EP5863	19971023			

AB The invention provides a granular **compn.** useful as a pharmaceutical carrier which can be used for the prepn. of pharmaceutical **compns.** that are capable of rapid suspension in **water** or **aq.** media including saliva. The **compns.** may be used by addn. to a glass of **water** with stirring or taken directly in the mouth. The granular **compn.** may be prepd. by a process which comprises subjecting a **mixt.** of a thickening agent and a disintegrating agent to wet granulation with an **aq.** medium as wetting agent or dry granulation to make a novel granular product and prepg. the pharmaceutical **compn.** from the granular product and the drug. A **water**-sol. inert excipient, which may be a sugar,

may be mixed with the granular product prior to mixing with the drug. Base granules were prepd. contg. Keltrol F, Ac-di-Sol, Avicel PH 200 and Explotab. These granules were mixed with Karion, aspartame and orange flavor and monodose sachets were prepd. from this **mixt.** and 5-aminosalicylic acid coated with Eudragit S.

IT **50-70-4**, Sorbitol, biological studies **57-48-7**, Fructose, biological studies **57-50-1**, biological studies **63-42-3**, Lactose **69-65-8**, D-Mannitol **115-77-5**, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical **compn.** for rapid suspension in **aq.** media)

IT **57-27-2**, Morphine, biological studies **58-32-2**, Dipyridamole **93-14-1**, Guaifenesin **103-90-2**, Paracetamol **114-07-8**, Erythromycin **3820-67-5**, Glafenine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **compn.** for rapid suspension in **aq.** media)

L78 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:123996 HCAPLUS
DN 128:184696
TI Easy to swallow oral medicament **composition**
IN Gruber, Peter
PA Losan Pharma G.m.b.H., Germany; Gruber, Peter
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806385	A1	19980219	WO 97-CH299	19970814
	W: AU, BG, BR, CA, CN, CZ, HU, JP, NO, PL, RO, RU, SI, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9736912	A1	19980306	AU 97-36912	19970814
PRAI	CH 96-2006		19960815		
	WO 97-CH299		19970814		

AB An easy-to-swallow pharmaceutical **compn.** consists of .gtoreq.1 coated particles with a core which contains an active substance and a coat with .gtoreq.1 layers. The coating layer(s) contains .gtoreq.1 hydratable, pharmaceutically acceptable polymer which, on contact with saliva or **water**, forms a coherent, moldable, viscous mass with a slippery surface which does not adhere to the mucous membranes of the mouth, and which prevents the active substance-contg. particles from leaving the mass and releasing the active substance in the mouth cavity. The (outermost) coating layer contains .gtoreq.1 salivation-promoting agent. The properties of the coating make the **compn.** suitable for administering highly dosed or bad-tasting active substances and even for swallowing without any liq. Thus, a soln. of ciprofloxacin 2000, Crospovidone XL-M 110, PVP K90 60, **water** 900, and EtOH 1800 g was spray-coated onto sucrose crystals 0.3-0.6 mm in diam. to produce core particles, which were then coated first with a powd. **mixt.** of

NaCl 50, Na saccharin 50, and Na carboxymethylstarch 50 g, and finally [after moistening with EtOH-H2O (1:1)] with a powd. **mixt** . of Na CM-cellulose 275 and talc 75 g.

IT **9004-62-0**, Hydroxyethylcellulose **9004-64-2**, Hydroxypropylcellulose **9004-65-3**, Hydroxypropylmethylcellulose **39421-75-5**, Hydroxypropyl guar gum
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coating, hydration of; easy-to-swallow oral medicament **compn** .)

IT **57-27-2**, Morphine, biological studies **60-54-8**, Tetracycline **103-90-2**, Paracetamol **114-07-8**, Erythromycin **4618-18-2**, Lactulose **15722-48-2**, Olsalazine **50679-08-8**, Terfenadine **51333-22-3**, Budesonide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(easy-to-swallow oral medicament **compn**.)

IT **50-70-4**, Sorbitol, biological studies **50-81-7**, L-Ascorbic acid, biological studies **50-99-7**, D-Glucose, biological studies **57-48-7**, D-Fructose, biological studies **57-50-1**, Sucrose, biological studies **69-65-8**, D-Mannitol **87-69-4**, Tartaric acid, biological studies **87-99-0**, Xylitol **134-03-2**, Sodium ascorbate **585-88-6**, Maltitol **14475-11-7 15421-15-5**, Potassium ascorbate **40968-90-9**, Potassium tartrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(easy-to-swallow oral medicament **compn**.)

L78 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112216 HCAPLUS
DN 128:184684
TI Novel stable liquid injectable paracetamol **compositions**
IN Dietlin, Francois; Fredj, Daniele
PA SCR Pharmatop, Fr.; Dietlin, Francois; Fredj, Daniele
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805314	A1	19980212	WO 97-FR1452	19970805
	W: AU, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RU, SG, US, VN				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2751875	A1	19980206	FR 96-9858	19960805
	FR 2751875	B1	19981224		
	CA 2233924	AA	19980212	CA 97-2233924	19970805
	AU 9739451	A1	19980225	AU 97-39451	19970805
	EP 858329	A1	19980819	EP 97-936739	19970805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FR 96-9858	19960805			
	WO 97-FR1452	19970805			

AB Novel stable paracetamol **compns**. for use in therapeutic chem. and specifically galenic pharmacy are disclosed. The **compns**. contain a soln. of paracetamol in an **aq**. solvent combined with a buffer having a pH of 4 to 8, and a free radical capturing agent. A

water-insol. inert gas is carefully bubbled through the **aq** . solvent to remove oxygen from the medium. Said **compns**. may also be combined with a centrally or peripherally acting analgesic agent, and are provided as injectable **compns**. for relieving pain. An injection soln. contained paracetamol 0.008, sodium chloride 0.008, disodium phosphate dihydrate 0.001, citric acid q.s. pH = 6.0, and **water** q.s. 1000 mL. The soln. kept at 98.degree. for 15 h showed no change of color and its absorbance at 500 nm was 0.016 as compared to 0.036 for the controls which were not packed under nitrogen and changed color.

IT **50-70-4**, Glucitol, biological studies **50-81-7D**, Ascorbic acid, alk. earth metal salts **50-81-7D**, Ascorbic acid, derivs. **50-99-7**, Glucose, biological studies **56-81-5**, Glycerol, biological studies **57-27-2**, Morphine, biological studies **57-48-7**, Levulose, biological studies **57-55-6**, Propylene glycol, biological studies **69-65-8**, Mannitol **87-89-8**, Inositol **96-27-5**, .alpha.-Thioglycerol **103-90-2**, Paracetamol **134-03-2**, Sodium ascorbate **3483-12-3**, Dithiothreitol **6055-06-7**, Morphine hydrochloride trihydrate **10504-35-5D**, D-Ascorbic acid, derivs. **25322-68-3**, Peg **62624-30-0D**, Ascorbic acid, alkali metal salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel stable liq. injectable paracetamol **compns**.)

L78 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:112214 HCAPLUS
DN 128:158943
TI Pleasant-tasting **aqueous** liquid **composition** of a bitter-tasting drug comprising polyvinylpyrrolidone
IN Anaebonam, Aloysius O.; Clemente, Emmett; Fawzy, Abdel A.
PA Ascent Pediatrics, Inc., USA; Anaebonam, Aloysius O.; Clemente, Emmett; Fawzy, Abdel A.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805312	A1	19980212	WO 97-US14018	19970807
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5763449	A	19980609	US 96-692081	19960807
	AU 9739132	A1	19980225	AU 97-39132	19970807
PRAI	US 96-692081	19960807			
	WO 97-US14018	19970807			

AB A liq. pharmaceutical **compn**. is claimed that comprises a pharmaceutically effective amt. of a bitter tasting drug dissolved or dispersed in an **aq**. medium that is free of ethanol. That **aq**. medium consists essentially of **water**, about 5 to about 30 wt. percent polyvinylpyrrolidone, about 35 to about 55 wt. percent of a C3-6 polyol, about 0.01 to about 0.5 wt. percent ammonium glycyrrhizinate and one or more flavorants. The liq. **compn**. is transparent and has a pleasant taste. A syrup contained guaifenesin 2.0,

PVP 7.5, glycerin 10.0, sodium benzoate 0.15, saccharin sodium 0.5, monoammonium glycyrrhizinate 1.0, anhyd. citric acid 0.25, sodium citrate 0.384, sodium alginate 0.2, maltitol syrup 20.0, **water**, flavors, colorants, and liq. 77.-77.5% fructose q.s. 100 mL.

IT **50-24-8** **50-70-4**, Sorbitol, biological studies **50-81-7**, Ascorbic acid, biological studies **51-43-4**, Epinephrine **57-27-2**, Morphine, biological studies **57-48-7**, Fructose, biological studies **58-56-0**, Pyridoxine hydrochloride **68-19-9**, Vitamin b12 **93-14-1**, Guaifenesin **103-90-2**, Acetaminophen **125-02-0**, Prednisolone sodium phosphate **130-40-5**, Riboflavin phosphate sodium **585-88-6**, Maltitol **18559-94-9**, Albuterol **50679-08-8**, Terfenadine **53956-04-0**, Ammonium glycyrrhizinate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pleasant-tasting **aq**. liq. **compn**. of bitter-tasting drug comprising polyvinylpyrrolidone)

L78 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:436459 HCAPLUS
DN 122:232781
TI Systematic toxicological analysis of basic drugs by gradient elution of an alumina-based HPLC packing material under alkaline conditions
AU Lambert, Willy E.; Meyer, Evelyne; De Leenheer, Andre P.
CS Lab. Toxicol., Univ. Gent, Ghent, B-9000, Belg.
SO J. Anal. Toxicol. (1995), 19(2), 73-8
CODEN: JATOD3; ISSN: 0146-4760
DT Journal
LA English
AB An HPLC system based on gradient elution from an alumina packing material coated with polybutadiene is presented. The chromatog. eluent is a gradient **mixt**. of MeOH and **H2O**, both contg. 0.0125M NaOH. The effluent is monitored by photodiode array detection. The system allowed detection and identification of 134 toxicol. relevant substances (mainly basic compds.) and has been successfully applied to screen >500 exts. of fresh or postmortem specimens (blood, urine, tissue homogenates, and stomach contents).
IT **57-27-2**, Morphine, analysis **103-90-2**, Acetaminophen **555-30-6**, Methyldopa **42200-33-9**, Nadolol
RL: ANT (Analyte); ANST (Analytical study)
(toxicol. anal. of basic drugs by HPLC, such as)

L78 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:186764 HCAPLUS
DN 120:186764
TI Shielded stationary phases for liquid chromatography or extn. of **mixtures** containing proteins and small analytes
IN Feibush, Binyamin; Gisch, Daryl J.
PA S.A.C. Corp., USA
SO U.S., 19 pp. Cont. of U.S. Ser. No. 557,333, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5277813	A	19940111	US 92-988610	19921210
PRAI US 88-208200		19880617		

US 90-557333 19900723

AB Novel packing materials are provided for liq. chromatog. and/or solid-phase extn. columns which will allow direct injection of biol. fluids for sepn. of small analytes from protein-contg. **mixts.** These packing materials have a hydrophilic exterior layer and a hydrophobic, charged, or otherwise selective portion that forms an underlayer or is embedded in the hydrophilic layer. During a chromatog. process, large **water**-sol. biopolymers will be in contact with the hydrophilic outer layer and be shielded from interacting with the underlayer or embedded portion and elute unretained. Small analytes, on the other hand, can be fully partitioned throughout the exterior and interior layers and are retained by hydrophobic or electrostatic interactions. Silica- and silica gel-bonded phases were prepd. [e.g., N,N-bis(2'-methoxyethyl)-11-(triethoxysilyl)undecylamine was prepd. and bonded to silica gel] and used in the direct analyses of drugs in plasma or serum samples.

IT **56-75-7**, Chloramphenicol **103-90-2**, Acetaminophen
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human blood serum by HPLC using shielded stationary phases)

L78 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1992:94 HCAPLUS
DN 116:94
TI Efficient extraction of basic, neutral, and weakly acidic drugs from plasma for analysis by gas chromatography-mass spectrometry
AU Brooks, Klazina E.; Smith, Norman B.
CS Dep. Clin. Biochem., Univ. Hosp., London, ON, N6A 5A5, Can.
SO Clin. Chem. (Winston-Salem, N. C.) (1991), 37(11), 1975-8
CODEN: CLCHAU; ISSN: 0009-9147
DT Journal
LA English
AB The authors described a method for efficiently extg. basic, neutral, and weakly acidic drugs from plasma for toxicol. anal. by gas chromatog.-mass spectrometry (GC/MS). The 2-mL plasma sample is dild. with an equal vol. of satd. NaCl contg. triethylamine, 10 mmol/L, and then extd. twice with 4 mL of an equivolume soln. of dichloromethane/acetone. The org. (top) phases are combined, then mixed with 1 mL of **water**, 200mg of NaHCO3, and 100 .mu.L of acetic anhydride. This **mixt.** is then heated at 75.degree. until the solvents have boiled off and **aq.** acetylation is complete (<30 min). After addn. of 1 mL of **water** and 2 g of NaCl, the sample is extd. twice with 2 mL of dichloromethane/acetone (2/1 by vol). The combined exts. are dried and then subjected to TLC on a blank Toxi-Lab Toxi-A chromatogram with 1-chlorobutane as the developing solvent (about 6 min). After the lipids have migrated with the mobile phase, the drugs are eluted from the origin with acetone/trimethylamine (29/1 by vol), evapd., and reconstituted in injection solvent. With this procedure drugs are recovered relatively quickly (<2 h) and the GC/MS total ion chromatograms are very clean. Studies with 13 basic, neutral, and weakly acidic drugs showed that all except theophylline were extd. with recoveries of at least 75%.

IT **57-27-2**, Morphine, analysis **103-90-2**, Acetaminophen
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human blood plasma by gas chromatog./mass spectrometry after extn. with thin-layer chromatog.)

L78 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 1999 ACS
AN 1991:520058 HCAPLUS

DN 115:120058
TI Effervescent dosage form and method of administering same
IN Wehling, Fred; Schuehle, Steve; Madamala, Navayanarao
PA Cima Labs, Inc., USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9104757	A1	19910418	WO 90-US5206	19900913
	W: AU, FI, HU, JP, KR, NO, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	AU 9066012	A1	19910428	AU 90-66012	19900913
	AU 646232	B2	19940217		
	EP 494972	A1	19920722	EP 90-915661	19900913
	EP 494972	B1	19961127		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 05500956	T2	19930225	JP 90-514500	19900913
	EP 737473	A1	19961016	EP 96-201072	19900913
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	AT 145551	E	19961215	AT 90-915661	19900913
	ES 2097155	T3	19970401	ES 90-915661	19900913
	US 5223264	A	19930629	US 91-750883	19910826
	CA 2061917	AA	19930827	CA 92-2061917	19920226
	US 5178878	A	19930112	US 92-869788	19920416
PRAI	US 89-416152	19891002			
	US 90-507642	19900411			
	EP 90-915661	19900913			
	WO 90-US5206	19900913			

AB Effervescent tablets comprise .gtoreq.1 effervescent disintegration agent in an amt. to aid rapid disintegration upon exposure to **water** or saliva and to provide a pos. organoleptic sensation. The disintegration agent is selected from the group consisting of citric acid, tartaric acid, malic acid, fumaric acid, adipic acid, succinic acid, and their anhydrides and salts. The tablets are esp. effective as oral pediatric dosage forms.
A tablet contg. 325 mg acetaminophen was prepd. by mixing and compressing following ingredients: acetaminophen 350.5, sorbitol 400.0, compressible sugar binding 400.0, citric acid 125.0, NaHCO3 100.0, cherry flavor powder 6.0, aspartame 40.0, KH2PO4 25.0, and lubricant 25.0 g.
IT **87-69-4**, biological studies **3019-59-8**, Tartaric anhydride
RL: BIOL (Biological study)
(effervescent tablet disintegration agents contg. carbonates and)
IT **50-81-7**, L-Ascorbic acid, biological studies
RL: BIOL (Biological study)
(effervescent tablet **formulation** of)
IT **65-23-6**, Pyridoxine **68-19-9**, Vitamin B12 **79-83-4**, Pantothenic acid **83-88-5 83-88-5**, Riboflavin, biological studies **103-90-2**, Acetaminophen
RL: PROC (Process)
(effervescent tablet **formulation** of)

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AN 1991:435728 HCAPLUS
DN 115:35728
TI Oral retard or repeat drug **formulation**
IN Khanna, Satish C.
PA Ciba-Geigy A.-G., Switz.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 408496	A2	19910116	EP 90-810498	19900703
	EP 408496	A3	19920701		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2020802	AA	19910113	CA 90-2020802	19900710
	JP 03063218	A2	19910319	JP 90-181700	19900711
PRAI	CH 89-2616		19890712		

AB A drug or drug **mixts.** is **formulated** with a noncolloidal material swellable in **water** and with a **water**-sol. osmosis-inducing material, and coated with a semipermeable membrane. Exposure to gastrointestinal juices causes, after a period of time, a sudden burst of the prepn., due to swelling and simultaneous onset of osmotic pressure. The prepn. allows for retard or repeat release of the drug, in a manner independent of the pH of and of the enzymes in the medium. A core comprising diclofenac Na 50, crosslinked PVP 100, NaCl 50, Aerosil-200 7, and Mg stearate 3 mg was coated with a **mixt.** of cellulose acetate (32% acetyl) 46.5, cellulose acetate (39.8% acetyl) 48.5, and hydroxypropylmethylcellulose 5.0 g.

IT **51-43-4**, Epinephrine **56-75-7**, Chloramphenicol **57-62-5**, Chlortetracycline **57-92-1**, biological studies **60-54-8**, Tetracycline **71-63-6**, Digitoxin **79-57-2**, Oxytetracycline **103-90-2**, Paracetamol **114-07-8**, Erythromycin **13292-46-1 20830-75-5**, Digoxin
RL: BIOL (Biological study)
(oral **formulation** of, retard and repeat)